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Analysis of Proteinuria in Urine Routine Examination During Urinary Tract Infection

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Abstract

Objective: This study was conducted to analyze the presence of proteinuria in urine routine examination during urine tract infection and its possible implications in patients admitted to Khan Research Laboratories (KRL) Hospital, Islamabad, Pakistan.

Method: The study enrolled 170 patients who were admitted in KRL Hospital during the year 2017, from January to December. This was a perspective, observational study. Statistical analysis was done using statistical package for social sciences (SPSS version 22).

Result: Out of 170 people there was loss of follow up of 34 patients. The mean age of patients was 54.81 ± 20.25 years. Females compromised of 65.3% and males compromised 34.7% of the patients. The study revealed there was no correlation between pus cells and proteinuria in urinary tract infection (r=0.132, p-value=0.086). There was statistically significant reduction in proteinuria after treatment (p-value <0.001). Incidence of proteinuria and pus cells during infection is positively correlated to female gender and age (p=0.001).

Conclusion: The presence of proteinuria during infection is not predictive of either the severity of infection or of an underlying renal pathology. Hence its repetition at the end of an infection to ensure clearance of proteinuria is not warranted; repeat urine routine examination should be decided on a case to case basis. However, based on the analysis done on both genders and different age groups it would be advisable to repeat urine routine examination at the end of infection for male patients particularly if they are of a younger age group.

Keywords: Urinary tract infection; Proteinuria; Urine repeat examination; Pus cells; Admission; Follow up

Introduction

Urinary tract infection (UTI) is one of the leading causes of infection worldwide. In United States urinary tract infection accounts for 8.3 million out-patient visits and 1 million hospitalizations every year [1]. In Britain, urinary tract infections account for 1%-3% of consultations [2]. Due to lack of computerization and proper documentation of patients' data in most hospitals of Pakistan, statistical analysis has not been done regarding the prevalence of urinary tract infection. However, inference from the statistics of developed countries suggests that the frequency of UTI would be high in Pakistan as well. In Khan Research Laboratories (KRL) hospital, Islamabad, Pakistan in year 2017, 8% of admissions in Medicine and Pediatric units were for urinary tract infection. This constitutes only a proportion of patients with this infection, as mostly this is treated in outpatient departments due to the uncomplicated nature of the disease. Hence, it indicates the high proportion of patients presenting with this infection in Pakistan.

Patients who present to outpatient department for urinary symptoms like frequency, burning and urgency usually undergo urine routine examination. Diagnosis of urinary tract infection requires the presence of pus cells in the urine [3,4]. Urinary tract infection is defined as the presence of 105 colony forming units (cfu)/mL in urine [5]. Infection is uncomplicated when there is no underlying anatomical or functional abnormality. The underlying bacteriology of urine tract infection is mainly compromised of gram negative pathogens, most common of which is Escherichia coli. The pathogenic spectrum is more diverse and resilient in people with underlying systemic or local renal pathology-indicating complicated infection [5,6].

Urine routine examination is an accessible, easy to perform, inexpensive test available throughout the country. It has also been called the poor man's renal biopsy. Besides indicating the presence of infection, urine routine examination is also a key investigation during workup for renal diseases like glomerulopathies, diabetic nephropathy, reflux nephropathy and tubular disorders. The sooner these diseases are diagnosed; better the prognosis in majority of cases. However the disease course of most of these diseases is silent and by the time patients present they are severely uremic and approaching end stage. The advantage of urine surveillance is that abnormalities are detectable in urine before derangements occur in the serum, allowing early disease identification- and more amenability to treatment [7]. Despite its established utility urine routine examination is still not used as a screening test in detection for renal pathologies. On the contrary, studies have suggestive urine routine examination is not a practical test for primary screening of renal disorders [8].

Urine analysis usually reveals presence of protein in addition to leukocytes during urinary tract infection [9-11]. Presence of this proteinuria is usually attributed to urinary tract infection, and overlooked [12,13]. Proteinuria is not a requirement for the diagnosis of urinary tract infection and its presence during urinary infection makes it an insensitive marker for another coexistent renal pathology. However inconsistency in its presence and in the amount of total proteinuria

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during infection raises the possibility of other factors besides infection which may influence this proteinuria during infection. Why some urine infections present with proteinuria and others do not, is still not fully established. Is there some correlation between the amount of proteinuria and the severity of infection? Does proteinuria occur only in severe infections or only in people with possible underlying renal pathology? If yes to latter then this would indicate the need to scrutinize this proteinuria further [14]. On the other hand some studies have postulated the presence of proteinuria due to the reaction of bacterial proteins with reagent strips, and not due to intrinsic renal defect; whether this is true, needs to be further verified [15].

Presence of protein in urine is one of the diagnostic features of intrinsic renal pathologies particularly glomerulopathies. Its presence is a predictor of ongoing progressive damage to kidney [16]. Significance of proteinuria is not restricted to kidneys only; this is also an indicator of increased risk of cardiovascular disease [17]. It has also been postulated that underlying renal impairment predisposes to urinary tract infection [18]; suggesting if a person presents with UTI and proteinuria the possibility of intrinsic renal pathology cannot be excluded. Usual clinical practice in evaluation of proteinuria is to rule out urinary tract infection by midstream urine culture first before further investigations; if culture positive then infection is treated before proceeding ahead in workup of proteinuria [19,20].

Due to infrequent outpatient visits and lack of follow up, it would be appropriate to fully utilize this opportunity when patients present with symptoms of urinary tract infection to scrutinize the urine routine examination and ensure the findings are due to urinary tract infection only, and not due to another coexistent renal pathology.

This study is a review of urine routine examinations of patients who were admitted in KRL hospital, Islamabad during the year 2017 for management of urinary tract infection. Presence or absence of proteinuria is assessed during urine tract infection. Thereafter patients were followed up to look for repeat routine urine examination after discharge to see if proteinuria cleared after infection was successfully treated. This study has been conducted to assess if the amount of proteinuria detected during urinary tract infection correlated with the severity of infection and the frequency of its persistence after clearance of pus cells.

Materials and Design

This is a perspective, observational study conducted in KRL hospital, Islamabad. The inclusion criterion was diagnosis of urinary tract infection on basis of urine routine examination and culture sensitivity report. Patients of ages 16 years and above were chosen. Patients were excluded if they were catheterized at time of sampling, had complicated diabetes mellitus or other known kidney diseases. Patients were informed about the study design and its implications; their record was selected after their consent.

SPSS version 22 was used for data management and analysis. Mean ± S.D was used for age and specific gravity and frequency distribution was used for categorical data like gender, number of pus cells, proteinuria and RBCs. For comparison of number of pus cell and proteinuria, spearman rank correlation was used and for comparison of parameters at admission with follow ups, Wilcoxon signed ranked test was applied for pair wise comparison. P-value ≤ 0.05 was considered as significant.

Results

The mean age of cases was 54.81 ± 20.25 years with minimum and maximum age 16 and 93 years. There were 43 (25.3%) cases with age 16-40 years, 58 (34.1%) cases were 41-60 years old and 69 (40.6%) cases were >60 years of age (Figure 1).

There were 59 (34.7%) male and 111 (65.3%) female cases in this study, showing female predominance (Figure 2).

On admission 3 (1.8%) cases had 4-8, 23 (13.5%) cases had 8-12, 11 (6.5%) had 12-16, 16 (9.4%) had 16-20, 34 (20.0%) cases had 20-24 and 83 (48.8%) cases had numerous pus cells. During follow up there were 68 (50%) cases who had 0-4 cells, 19 (14%) cases had 4-8 cells, 10 (5.9%) cases had 8-12 cells, 5 (3.7%) cases had 12-16 cells, 3 (2.2%) cases had 16-20 cells, 10 (7.4%) cases had 20-24 and 21 (15.4%) cases had numerous pus cells.

The pus cells statistically reduced after treatment, p-value <0.001. At admission there were 90 (52.9%) cases who had no Proteinuria, 17 (10%) cases had Faint trace, 21 (12.4%) cases had Trace, 19 (11.2%) cases had +Proteinuria, 17 (10%) cases had ++Proteinuria and 6 (3.5%) had +++proteinuria. After treatment a total of 93 (68.9%) case had Nil, 14 (8.2%) cases had Faint trace, 10 (5.9%) cases had Trace, 10 (5.9%) cases had +Proteinuria, 6 (3.5%) cases had ++Proteinuria and 2 (1.2%) cases had +++Proteinuria. There was statistically significant reduction in proteinuria after treatment, p-value <0.001 (Tables 1-6).

Among cases of diagnosed UTI, 90 (52.9%) cases had no proteinuria (in which 3 cases had 4-8, 11 cases had 8-12, 5 cases had 12-16, 10 cases

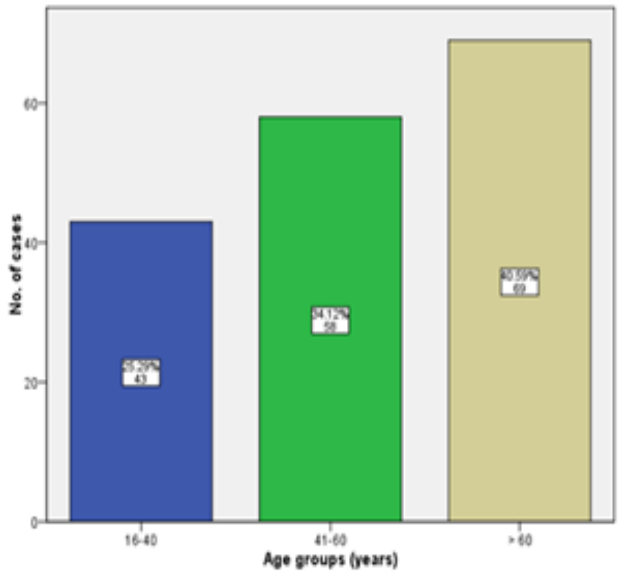

Figure 1: Mean age of cases with minimum and maximum age 16 and 93.

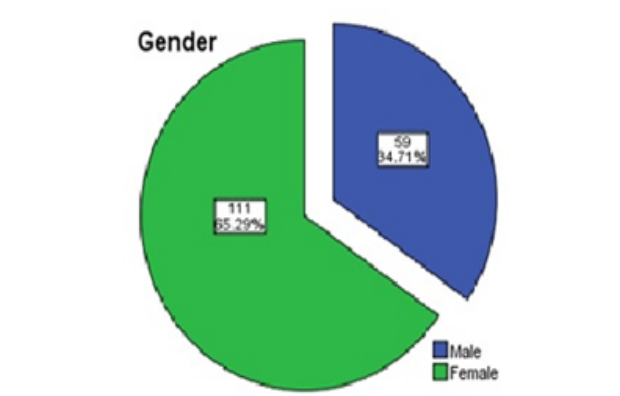

Figure 2: Percentage of Male and Female cases in the study.

		On Admission (n=170)	At Follow-up (n=135)	p-value
Pus Cells	0-4	0 (0%)	68 (50%)	<0.001
	04-Aug	3 (1.8%)	19 (14%)	
	08-Dec	23 (13.5%)	10 (5.9%)	
	Dec-16	11 (6.5%)	5 (3.7%)	
	16-20	16 (9.4%)	3 (2.2%)	
	20-24	34 (20.0%)	10 (7.4%)	
	Numerous	83 (48.8%)	21 (15.4%)	
Proteinuria	Nil	90 (52.9%)	93 (68.9%)	<0.001
	Faint trace	17 (10%)	14 (8.2%)	
	Trace	21 (12.4%)	10 (5.9%)	
	+	19 (11.2%)	10 (5.9%)	
	++	17 (10%)	6 (3.5%)	
	+++	6 (3.5%)	2 (1.2%)	
RBCs	Nil	40 (23.5%)	59 (34.7%)	0.09
	0-2	40 (23.5)	29 (17.1%)	
	02-Apr	30 (17.6%)	20 (11.8%)	
	04-Jun	12 (7.1%)	11 (6.5%)	
	06-Aug	16 (9.4%)	8 (4.7%)	
	08-Oct	9 (5.3%)	1 (0.6%)	
	10-Dec	1 (0.6%)	1 (0.6%)	
	Dec-15	3 (1.8%)	3 (1.8%)	
	15-20	5 (2.9%)	0 (0%)	
	25-30	2 (7.1%)	0 (0%)	
	Numerous	12 (7.1%)	3 (1.8%)	
Specific gravity	Mean ± S.D	1012.71 ± 7.48	1013.30 ± 6.75	

Table 1: Comparison of Pus cell, Proteinuria, RBCs and Specific gravity at admission and follow up.

		Proteinuria (On Admission)					
		Nil	Faint Trace	Trace	+	++	+++
Pus cells	04-Aug	3	0	0	0	0	0
(On Admission)		100%	0%	0%	0%	0%	0%
	08-Dec	11	2	4	6	0	0
		47.82%	8.69%	17.39%	26.08%	0%	0%
	Dec-16	5	1	4	1	0	0
		45.45%	9.09%	36.36%	9.09%	0%	0%
	16-20	10	2	3	1	0	0
		62.50%	12.50%	18.75%	6.25%	0%	0%
	20-24	21	5	1	2	4	1
		61.76%	14.70%	2.94%	5.88%	11.76%	2.94%
	Numerous	40	7	9	9	13	5
		48.19%	8.43%	10.84%	10.84%	15.66%	6.02%
Total		87	17	21	19	17	6

Table 2: Comparison of number of Pus Cells and Proteinuria on admission.

		Proteinuria
Pus cells	Spearman's rho	0.132
	p-value	0.086 (insignificant)
	No. of cases	170

Table 3: Correlation of Proteinuria with Pus cells at admission.

had 16-20, 21 cases had 20-24 and 40 cases had numerous pus cells) (Tables 7-11). So, there was no statistically significant correlation of number of pus cells and proteinuria spearman correlation (r=0.132, p-value=0.086). Stratification of data based on genders and age groups revealed that proteinuria and pus cells in urine routine examination on admission were more in females and in old age groups (p=0.001) and were statistically significant.

Discussion

This study consisted of 170 cases who were admitted in KRL hospital for urinary tract infection in the year 2017. Out of these there was a loss of follow up of 34 cases. Analysis of the data revealed there was no correlation between the amount of pus cells and the accompanying proteinuria during infection(r=0.132, p-value=0.086). Later treatment of infection cleared the proteinuria significantly (p<0.001) suggesting that the proteinuria was due to infection as postulated by earlier studies [12,13] and, is not suggestive of underlying renal pathology as concluded by some other studies [14,18]. It is advised to follow up patients with urinary tract infection with repeat urine routine examination to ensure clearance of infection [21,22]. This study negated the routine need for repeat investigation.

The hypothesis that kidneys susceptible to future impairment are more likely to produce proteinuria can only be substantiated by following the people with significant proteinuria during urinary tract infection long term to assess if they do actually develop an intrinsic renal

		Proteinuria (on Follow-up)					
		Nil	**Faint Trace**	**Trace**	**+**	**++**	**+++**
Pus cells (on Follow-up)	4-8	56	5	3	3	0	0
		83.58%	7.46%	4.47%	4.47%	0%	0%
	8-12	14	2	2	0	1	0
		73.68%	10.52%	10.52%	0%	5.26%	0%
	12-16	8	2	1	0	0	0
		72.72%	18.18%	9.09%	0%	0%	0%
	16-20	2	0	2	1	0	0
		40%	0%	40%	20%	0%	0%
	20-24	0	0	0	2	0	1
		0%	0%	0%	66.66%	0%	33.33%
	Numerous	6	3	0	0	1	0
		60%	30%	0%	0%	10%	0%
Total		86	12	8	6	2	1
		74.78%	10.43%	6.95%	5.21%	1.73%	0.86%

Table 4: Correlation of Proteinuria with Pus cells on Follow-up.

		Proteinuria
Pus cells	p-value	0.001 (significant)
	No. of cases	136

Table 5: Correlation (p-value) of Proteinuria with Pus cells on Follow-up.

		Pus cells (on Admission)							Total
		0-4	**4-8**	**8-12**	**12-16**	**16-20**	**20-24**	**Numerous**	
Gender	Male	0	2	9	2	5	9	31	58
		0%	3.44%	15.51%	3.44%	8.62%	15.51%	53.44%	99.96%
	Female	0	2	15	9	11	26	49	112
		0%	1.78%	13.39%	8.03%	9.82%	23.21%	43.75%	99.98%
Total		0	3	24	11	16	34	80	168
		0%	1.78%	14.28%	6.54%	9.52%	20.23%	47.61%	99.96%
P-value=0.001 (significant)									

Table 6: Correlation between Pus cells and Gender on Admission.

		Pus cells (on Admission)							Total
		0-4	**4-8**	**8-12**	**12-16**	**16-20**	**20-24**	**Numerous**	
Age groups (years)	16-40	0	0	7	3	1	11	14	36
		0%	0%	19.44%	8.33%	2.77%	30.55%	38.88%	99.97%
	41-60	1	8	5	5	9	9	30	67
		1.49%	11.94%	7.46%	7.46%	13.43%	13.43%	44.77%	99.98%
	>60	0	2	7	3	8	14	33	67
		0%	2.98%	10.44%	4.47%	11.94%	20.89%	49.25%	99.97%
Total		1	10	19	11	18	34	77	170
		0.58%	5.88%	11.17%	6.47%	10.58%	20%	45.29%	99.97%
P-value=0.001 (significant)									

Table 7: Correlation between Pus cells and Age groups on Admission.

		Pus cells (on Follow up)							Total
		0-4	**4-8**	**8-12**	**12-16**	**16-20**	**20-24**	**Numerous**	
Age groups (years)	16-40	18	3	4	1	1	3	5	35
		51.42%	8.57%	11.42%	2.85%	2.85%	8.57%	14.28%	99.96%
	41-60	20	8	1	1	1	3	7	41
		48.78%	19.51%	2.43%	2.43%	2.43%	7.31%	17.07%	99.96%
	>60	30	8	5	3	1	4	9	60
		50%	13.33%	8.33%	5%	1.66%	6.66%	15%	99.98%
Total		68	19	10	5	3	10	21	136
		50%	13.97%	7.35%	3.67%	2.20%	7.35%	15.44%	99.98%
P-value=0.965 (insignificant)									

Table 8: Correlation between Pus cells and Age groups on Follow up.

		Pus cells (on Follow up)							Total
		0-4	4-8	8-12	12-16	16-20	20-24	Numerous	
Gender	Male	26	10	3	2	2	0	8	51
		50.98%	19.60%	5.88%	3.92%	3.92%	0%	15.68%	99.98%
	Female	42	9	7	3	1	10	13	85
		49.41%	10.58%	8.23%	3.52%	1.17%	11.76%	15.29%	99.96%
Total		**68**	**19**	**10**	**5**	**3**	**10**	**21**	**136**
		50%	13.97%	7.35%	3.67%	2.20%	7.35%	15.44%	99.98%
P-value=0.162 (insignificant)									

Table 9: Correlation between Pus cells and Gender on Follow up.

		Proteinuria (on Admission)						
		Nil	Faint trace	Trace	+	++	+++	Total
Age Groups (years)	16 to 40	28	4	2	5	4	0	43
		65.11%	9.30%	4.65%	11.62%	9.30%	0%	99.98%
	41 to 60	32	4	9	5	6	2	58
		55.17%	6.89%	15.51%	8.62%	10.34%	3.44%	99.97%
	>60	31	8	10	9	7	4	69
		44.92%	11.59%	14.49%	13.04%	10.14%	5.79%	99.97%
Total		**91**	**16**	**21**	**19**	**17**	**6**	**170**
		53.52%	9.41%	12.35%	11.17%	10%	3.52%	99.97%
P-value=0.001 (significant)								

Table 10: Correlation between Proteinuria and Age groups on Admission.

		Proteinuria (on Admission)						
		Nil	Faint trace	Trace	+	++	+++	Total
Gender	Male	27	6	6	10	4	5	58
		46.55%	10.34%	10.34%	17.24%	6.89%	8.62%	99.98
	Female	64	10	15	9	13	1	112
		57.14%	8.92%	13.39%	8.03%	11.60%	0.89%	99.97%
Total		**91**	**16**	**21**	**19**	**17**	**6**	**170**
		53.52%	9.41%	12.35%	11.17%	10%	3.52%	99.97%
P-value=0.001 (significant)								

Table 11: Correlation between Proteinuria and Gender on Admission.

pathology. Alternatively, people with intrinsic renal pathology can be followed retrospectively to see if they developed significant proteinuria during a urinary tract infection in the past-provided they ever had this infection. But considering the incidence of this infection worldwide the former option would not be practical economically and will place a heavy burden on the infrastructure. However the latter option is worth consideration and a subject for future research.

During this study urine tract infection was solely represented by pus cells in the urine and while proteinuria was a frequent accompanying occurrence it did not add to the severity of infection nor did it alter the treatment course. This indicates that following such people with repeat evaluation is not warranted both medically or financially just to ensure clearance of proteinuria.

However, another important consideration is the physiological characteristics of the patients-according to this study female population had a higher proportion of infection, pus cells and proteinuria. Age was also a limiting factor-higher the age higher the incidence of pus cells and proteinuria. These were statistically significant ($p<0.001$). If the results of this study are applied, it would seem important to ensure clearance of proteinuria and infection in a male patient especially if he is of a relatively young age because the presence of these two is against the normal physiological pattern seen based on the data of this study. Similar approach is suggested by other studies as well [23].

However, this study does have its limitations: About 20% of the patients had loss of follow up-suggesting a substantial percentage of lost data. This study needs to be conducted on a larger group of people to ensure that despite loss of follow up, there is still a significant proportion of follow up data to substantiate the results. Another important point is that this study dealt with patients who had uncomplicated urinary tract infection. Hence the results could not be applied to patients with any anatomical or functional renal impairment- that is complicated urinary tract infection.

Conclusion

In conclusion, based on the results of this study; presence of proteinuria in urine routine examination during uncomplicated urinary tract infection is a common and benign occurrence; it is not suggestive of an intrinsic renal pathology nor is it an indicator of infection severity. However the decision to follow up patients should be done on an individualized basis. Male gender and a younger age group are generally less susceptible to this infection and if infected should be followed up to ensure there is no concomitant renal pathology or complicated infection.

Conflict of Interest

The study has no conflict of interest to declare by any author.

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