The effect of oral hypoglycemic agents in the Urine Cytology of Females with Type II Diabetes Mellitus.

Dr.Mutasim .S. Mohammed Salih[1], Mohammed.F. Khalid([2]),Asaad.A. Almsaad([3]) and Salma. O.Hussin([4])

مستخلص البحث

الخلفية: علم خلايا البول هو أكثر اختبار غير تدخلي استخداما على نطاق واسع في الكشف عن الظهارة البولية غير نمطية التغيير (ذات التغيير النموذجي) . ومع ذلك فهو محدود نسبة لحساسيته المنخفضة خاصة في الكشف عن أورام الظهارة البولية ولكن يمكن أن يكون مفيدا في تحديد التغيرات مثل حالات الالتهابات. وبناء على ذلك، تهدف هذه الدراسة إلى تحديد الالتهابات والأورام (إن وجدت) والتي قد تنتج من اثر العلاج الدوائي الفموي لمرض سكر الدم لدى الإناث المصابات بالنوع الثاني من مرض السكر (DM).أجريت هذه الدراسةُ الوصفية و المقارنة في مسِتشفى كوستى التعليمي في الفترةِ مِنْ شهر يناير إلى شهر مارس للعام ٢٠٠٩ وقد هدّفتْ لتحديد تأثيرَ نوعِ داء السكّري الثّاني على الغشاء المخاطي في الجهاز البولي بين الإناث المصابات بالنوع الثاني من مرض السكر وقياس اثر العلاج الفموي للمرض على ذلك .

منهجية البحث: تم ادخال 100 من النساء المصابات بالنوع الثاني من السكر لهذه الدراسة عن طريق الاختيار العشوائي بغض النظر عن أعمارهن وأعراقهن. تم جمع عينة بول من كل منهن في إناء معقم وتم تجهيز العينات وصبغها بطريقة (بابانيكلو).

النتائج : 60 منهن يمثلن 60 في المائة وجدن مصابات بتسرب الخلايا الالتهابية .وقد وجد أن هذه التغيرات في الخلايا تتناسب طرديا مع فترة الإصابة بالمرض والأدلة على وجود خلايا تشير للإصابة بالبكتريا تم التعرف عليها لدى 52 مريضة بنسبة 61.2 في المائة و 31 مريضة بنسبة 72.1 في المائة منهن تحت العلاج الصيدلاني من الفقيرات اجتماعيا واقتصاديا.

الخاتمة: وجد أن نسبة الإصابة بالالتهابات في المجارى البولية مرتفعة عند الإناث اللائي يعالجن من داء السكر وكذلك الفقيرات منهن.

Abstract

Setting: Urine cytology is the most widely used non invasive test to detect urothelial atypical changes. Though, it is limited by its low sensitivity, particularly in the detection of urothelial tumors, but it can be useful in identification of changes such as inflammatory conditions. Therefore, This study was conducted at Kosti Teaching Hospital January- March 2009 and it aimed to assess the inflammatory, metaplastic and neoplastic (if any) that might results from the effect of pharmacologic treatment-oral hypoglycemic agents in females with diabetes mellitus (DM) type II. **Material and Methods**: One hundred women with DM type II were recruited for this study by simple random method regardless of their ages and ethnicities. Full voided urine specimen was collected in sterile urine container and prepared to be stained according to Papanicolaou method. **Results:** Out of 100 cases, 60 (60%) were found with inflammatory cell infiltrates. These inflammatory cells were found to increase with

[1]- Head Department of Clinical Pharmacology- Faculty of Medicine- Al Imam Al Mahdi University.
2,3,4 Ministry of health- the White Nile State- Department of laboratory- Histology and Cytology.

increasing the duration of the disease. Cytological evidences of bacterial infection were identified among 52 (61.2%) and 31 patients (72.1%), of those under pharmacologic treatment and poor socioeconomic status respectively. Cytological atypia was not found. **Conclusion:** Inflammatory infiltrate was common amongst patients with DM type II. The elevation in risk of urinary tract infections among type II diabetic women was mainly present in those who were on treatment. Further studies to investigate the relation between bacterial infection and the type of inflammatory infiltrate are recommended.

Key words: Urine cytology, oral hypoglycemic agents, diabetes mellitus

Introduction

Normally, urine contains few urothelial cells and non cellular materials such as; casts, crystals, and corpora amylacea in males. Squamous cells may be seen in urine, especially in females, originated from trigone of bladder or as a contaminant from the vagina. [1] Urinary Tract Bacterial infections are common in females rather than males. This infection is commonly caused by Escherichia coli, proteus, and klebsiella species. Therefore, urine for culture is necessary for identification. [2]

The occurrence of Urinary tract infection (UTI) varies with age and sex, the predisposing factors include diabetes mellitus, foreign bodies, recent instrumentation of the urinary tract, neurological disorders or drugs that may cause incomplete emptying of the bladder, Co-existing diseases involving the pelvis and sexual activity. If UTI is left untreated, the infection can spread upwards to the kidneys, causing infection in the kidneys and even renal failure. It can also spread via the blood stream to affect the body in general, which may be fatal. [3]

Early studies revealed that there were no significant differences in the prevalence of bacteriuria between men with diabetes and men without diabetes. In contrast, the prevalence of asymptomatic bacteriuria is two to three times as high among women with diabetes as among women without diabetes, and the frequency of symptomatic urinary tract

infections is higher among women with diabetes than among those without diabetes.[4], [5]

Furthermore, local studies have shown that infection of the upper urinary tract at initial testing is more common among women with bacteriuria and diabetes (occurring in 63 percent) than among women with bacteriuria but no diabetes (43%). [6], [7]

Also there were high prevalence of genitourinary structural abnormalities among women with diabetes who have recurrent UTI (30 %) than among non diabetic women with such infections (4 %).[8] An increased prevalence of UTI and asymptomatic bacteruria has been described in women with diabetes compared to women without diabetes. [9] Diabetes results in several abnormalities of the host defense system that might result in a higher risk of certain infections [10], [11].

The elevation in risk of urinary tract infections among diabetic women was mainly present in those under pharmacologic treatment to reduce. Diabetes is associated with a higher risk of acute symptomatic UTI in postmenopausal women. Women undergoing pharmacologic treatment for diabetes were mainly at higher risk, suggesting an association between severity of diabetes and risk of UTI. [12], [13], [14], [15], [16]

Although the relation between diabetes and asymptomatic bacteriuria has been the subject of several controlled studies, the association between diabetes and urinary tract infection risk has not been examined earlier. [17]

Higher risk of UTI was expected with longer duration of diabetes [18], [19], [20].

The frequency of UTI has been shown to be increased only in diabetic women compared with non-diabetic women, but not in diabetic men compared with non-diabetic men. This difference may be secondary to the increased incidence of virginities among women with diabetes mellitus. [21]

Diabetes causes several abnormalities of the host defense system that might result in a higher risk of certain infections, including UTI including immunologic impairments, such as impaired migration, intracellular killing, phagocytosis, and chemotaxis of polymorphonuclear leukocytes from diabetic patients and neuropathic complications, such as impaired bladder emptying In addition, a higher glucose concentration in the urine may create a culture medium for pathogenic microorganisms. [22] ،[23], [24].

Diabetic women had significantly higher risks of overall UTI and a first episode of asymptomatic bacteriuria, higher risk of acute symptomatic UTI and asymptomatic bacteriuria among postmenopausal women with diabetes. Women taking insulin were mainly those at higher risk, possibly because of more severe diabetes, since the use of insulin may be a marker for disease severity. [25]. Therefore, this study aimed to assess the effect of diabetes mellitus type II, on the mucosa in UTI, among females at Kosti teaching hospital.

Materials and methods:

This is a descriptive study conducted at Kosti teaching hospital, between January to March 2009.

Urine samples were taken from 100 females with diabetes mellitus type II who agreed to participate in this study. Individuals were grouped according to the duration of type II diabetes mellitus as following: (i) group I (< 5 years of duration) (ii) group II (5 to 10 years of duration). 70 patients from group I and 30 patients from group II were recruited to take place in this study. Information on age, duration of disease, use of treatment, socioeconomic status and material status were taken from each individual.

The urine sample was collected as full voided urine (neither early morning nor midstream) in a clear, dry, sterile containers. [29], centrifuged immediately at 1500 rpm for 10 minutes, the supernatant poured off, then

the deposit was mixed with a drop of albumin, the suspensions was removed using a pipette and a single small drop was placed towards the end of a clean, labeled glass slide and separate rapidly. Cells in the urine degenerate rapidly therefore smear should be prepared and fixed immediately. The smear fixed immediately in 95% ethanol for 15 minutes. [29]

Samples were stained by papanicolaou staining method, the alcohol fixed smears were dehydrated in decreasing alcohol concentration of 95% ethanol through 70% ethanol to distilled water for two minutes in each stage. Then stained with Harris's Haematoxylin for five minutes after that rinse in water for two minutes, were differentiated in 0.5% aqueous HCL , rinsed in water for two minutes , blue in Scott's tab water substitute two minutes, rinsed in water for two minutes, dehydrated in 70% alcohol for two minutes, used 95% alcohol two minutes, stained in O.G.6 for two minutes, , rinsed in 95% alcohol for two minutes, stained in EA 50, for three minutes, rinsed in 95% alcohol for one minutes, Dehydrate in alcohol , cleared in Xylene and mounted in DPX medium. [29]

Smears were ready to be examined by light microscope for the assessment of different cells appearance in the smears.

Data were analyzed, using computer SPSS program.

Each individual was told about the research importance during the interview and all of them were agreed to participate in this study.

The Results

Table (1) Categorization of the study population

Variables	**study population %**

Table (2) The Prevalence of urine cytological changes in diabetic Females regarding to the duration of the disease

Duration of the disease	Less than 5 years	70 %
	5 - 10 years	30 %
On treatment	Yes	85 %
	On and Of treatment	15 %
Socioeconomic status	Poor	43%
	Not poor	57%
	Single	10%

			Result		
			Normal	Bacterial infection	Total
Duration of diabetes	less than 5 years	Bacterial Cells /Field	30	40	70
		%	42.9%	57.1%	100.0%
	5-10 years	Bacterial Cells /Field	10	20	30
		%	33.3%	66.7%	100.0%
Total		Bacterial Cells /Field	40	60	100
		%	40.0%	60.0%	100.0%

Table (3) The Prevalence of Cytological changes in diabetic Females Regarding the use of hypoglycemic agents

		Result		
		Normal	Bacterial Infection	Total
On regular treatment	Bacterial Cells /Field	33	52	85
	% within Result	82.5%	86.7%	85.0%
Irregular treatment		7	8	15
	% within Result	17.5%	13.3%	15.0%
Total	Bacterial Cells /Field	40	60	100
	% within Result	100.0%	100.0%	100.0%

Table (4) The prevalence of urine cytological changes in diabetic Females according to the socioeconomic status

			Result		
			Normal	Bacterial infection	Total
Socioecnomic status	Poor	Bacterial Cells /Field	12	31	43
		% within Socioeconomic status	27.9%	72.1%	100.0%
		% within Result	30.0%	51.7%	43.0%
	Not poor	Bacterial Cells /Field	28	29	57
		% within Socioeconomic status	49.1%	50.9%	100.0%
		total	70.0%	48.3%	57.0%
Total		Bacterial Cells /Field	40	60	100
		%	40.0%	60.0%	100.0%
		total	100.0%	100.0%	100.0%

Table (5) The prevalence of urine cytological changes in the diabetic Females according to the marital status

			Result		
			Normal	Bacterial infection	Total
Marital status	Single	Count	5	5	10
		% within Marital status	50.0%	50.0%	100.0%
		% within Result	12.5%	8.3%	10.0%
	Married	Count	30	43	73
		% within Marital status	41.1%	58.9%	100.0%
		% within Result	75.0%	71.7%	73.0%
	Separate	Count	5	12	17
		% within Marital status	29.4%	70.6%	100.0%
		% within Result	12.5%	20.0%	17.0%
Total		Count	40	60	100
		% within Marital status	40.0%	60.0%	100.0%
		% within Result	100.0%	100.0%	100.0%

The Discussion

Urine cytology is usually used for tumor detection and diagnosis of aggressive neoplasm, or their flow-up, carcinoma in situ, small or inaccessible lesion as in ureter and pelvis, for screening of high-risk asymptomatic patients . **Hence**, it has a potential value in assessment of different renal abnormalities. [7]

It was reported that inflammatory change as bacterial infections were more prevalent in the urine of females with diabetes mellitus type II who got the disease in the duration of 5-10 years, when compared to those who got it in less than 5 years table(1), which is similar to the results reported by Geerlings SE, and coworkers, Edward J. and coworkers 2005,and Harris M.1995 [24], [25] [28]

This study showed that more prevalent bacterial infection in the group of Females who are on regular treatment (86.7%) , when compared to those who use the treatment in on and off way table (3), same result were reported by Edward J and coworkers 2002,Stein G, and Fünfstück R. 1999, Geerlings SE and coworkers, Edward J. and coworkers2005 , Boyko EJ, and coworkers 2002 [22], [23], [24], [25], [26]

The prevalence of normal cytology, in the collected samples from females with diabetes mellitus type II, in not poor socioeconomic status group, represent 70%, compared with the other socioeconomic status grouptable (4).

This study showed more prevalence of bacterial infection in married group, represent 71.7%, compared with the other marital status groups table (5).which is similar to the results that were reported by Suzanne E nd coworkers 2000 [29]

70% of study population is less than 5 years in duration of type II diabetes mellitus, so no remarkable fungal infection or metaplastic changes in the cytomorphology of urine samples of the study population.

Conclusion

In conclusion, diabetes mellitus type II is associated with inflammatory changes especially bacterial infections in the mucosa of urinary tract. Not only this, but also these Inflammatory changes are affected with the duration of the Disease.

The risk of UTI among type II diabetic women was mainly high in those who are treated with hypoglycemic agents.

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