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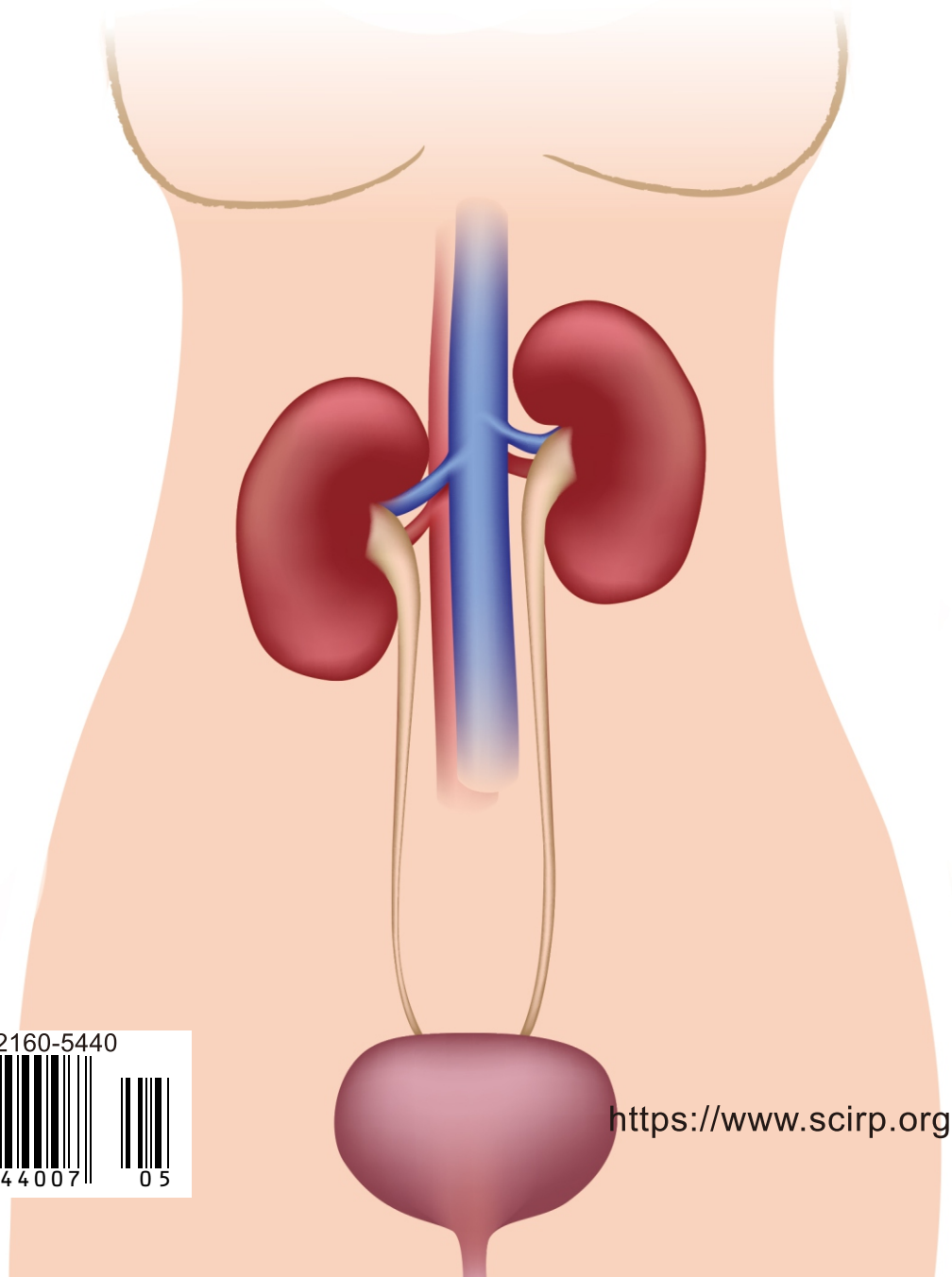

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Table of Contents

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Plasma Levels of Transforming Growth Factor-Beta 1 in Women with Pelvic Organ Prolapse

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Abstract

Objective: In women with pelvic organ prolapse (POP), decreased expression of transforming growth factor-beta 1 (TGF-β1) has been shown in POP tissues. However, no studies have evaluated plasma TGF-β1 levels in patients with POP, so it is unknown whether they are also changed or not. Therefore, we compared plasma TGF-β1 levels in women with and without POP. **Methods**: Participants were 49 women with POP and 23 healthy control women. All participants were postmenopausal. We measured plasma TGF-β1 and compared data between patients with POP and controls, and between patients with uterine prolapse (UP, n = 19) and those with a cystocele (CC, n = 30). In addition, in patients, we assessed the POP quantification system (POP-Q) stage. **Results**: Plasma TGF-β1 levels were significantly lower in patients than in healthy controls. POP-Q stage was not significantly different between the UP and CC subgroups, but POP-Q stage IV was diagnosed in 63% of patients with UP and 7% of those with CC. Plasma TGF-β1 levels were significantly lower in the CC subgroup than in the UP subgroup. **Conclusion**: Plasma TGF-β1 is decreased in POP. It remains unclear whether the lower levels indicate a reduction in systemic TGF-β1 activity, but they can be assumed to reflect reduced TGF-β1 expression in POP tissues.

Keywords

Cystocele, Pelvic Organ Prolapse, Transforming Growth Factor-Beta 1 (TGF-β1), Uterine Prolapse

1. Introduction

Pelvic organ prolapse (POP) is characterized by the weakening of pelvic supportive tissue in women, which leads to prolapse of the uterus, bladder, and rectum outside the pelvis through the vagina [1]. POP, which is more common in older women, affects approximately 9% of women worldwide and greatly impacts their quality of life [2] [3]. A large community-based retrospective cohort study identified factors that increase the risk of POP, *i.e.* older age, postmenopausal status, higher parity, elevated intraabdominal pressure, and overweight [4] [5] [6]. In addition, a combination of support defects in the anterior, posterior, and apical vaginal segments and abnormalities of connective tissue structure or its repair mechanism might predispose women to develop POP [4] [5] [7]. Recent studies on POP have focused on the abnormal structure and organization of pelvic floor connective tissue and the molecular alterations in uterosacral ligaments [8] [9] [10]. Notably, a breakdown of the extracellular matrix is commonly reported [11] [12], and this process was shown to decrease the strength of supportive structures and contribute to the pathogenesis of POP [13] [14]. However, the exact molecular mechanisms underlying the breakdown of the extracellular matrix are not yet fully understood.

The cytokine transforming growth factor-beta 1 (TGF-β1) remodels the extracellular matrix by regulating multiple enzymes and extracellular matrix components [15]. In women with POP, decreased expression of TGF-β1 has been shown in fibroblasts, the pubovaginal fascia, and cardinal ligament tissues [16] [17] [18] [19] [20]. The expression level of TGF-β1 is positively correlated with collagen expression [20], so low levels of TGF-β1 expression might be associated with the occurrence of POP. To date, no studies have evaluated plasma TGF-β1 levels in patients with POP, so it is unknown whether they are also decreased. Therefore, this study compared plasma TGF-β1 levels in women with POP and healthy control women.

2. Participants and Methods

Participants (N = 72) were 49 female patients (49 - 85 years old) who were diagnosed with POP between December 1, 2011 and March 31, 2013, and 23 healthy female controls (49 - 75 years old). Patients were selected from women attending a consultation at the Department of Urology at Okinawa Kyodo Hospital for that period. POP and POP quantification system (POP-Q) stage [21] were diagnosed by cystography and pelvic examination, and patients were asked whether they had stress urinary incontinence. Inclusion criteria for the POP patient group included POP-Q stage 2 or greater prolapse, as assessed by a single physician (K.K), and a plan for surgery by the same physician to treat the symptomatic prolapse. Healthy controls were volunteers without urinary tract symptoms who were recruited from Kitakami Central Hospital staff (nurses, helpers, and clerks) and their families for the period between December 1, 2012 and March 31, 2013.

All participants were postmenopausal and had no other urological or gynecological illnesses, diabetes, or hypertension. In all participants, blood was drawn at study visits, outpatient visits, or on admission for surgery, and plasma TGF-β1 was measured by enzyme-linked immunosorbent assay (SRL, Inc., Tokyo, Japan). Height, body weight, and body mass index (BMI) were also measured. Data were compared between patients with POP and healthy controls and between patients with uterine prolapse (UP) and those with a cystocele (CC).

This was a multicenter clinical study. The study was approved by the ethics committee of Okinawa Kyodo Hospital on behalf of all participating institutions (approval No. 2010-005). Before enrollment, all participants were given a detailed explanation of the objectives and methods of the study and gave their written consent.

Results are expressed as the mean ± standard deviation (SD). The unpaired *t* test was used for statistical analysis, and the p-value of less than 0.05 was used as the threshold for significance.

3. Results

Although all participants were postmenopausal, the healthy controls were significantly younger than the patients (Table 1). They were also significantly taller, but body weight and BMI were not significantly different between the two groups. In healthy controls, plasma TGF-β1 levels did not correlate with age, height, weight, or BMI (Table 2). Plasma TGF-β1 levels were significantly (p = 0.027) lower in patients (6.3 ± 3.6 ng/mL) than in healthy controls (8.1 ± 5.7 ng/mL) (Figure 1).

Table 1. Basic characteristics of women with pelvic organ prolapse (POP) and healthy control women (Controls).

	Controls (n = 23)	POP patients (n = 49)	p-value
Age (years old)	56.4 ± 7.5	66.3 ± 8.6	<0.001
Height (cm)	154.1 ± 3.7	148.5 ± 5.4	0.010
Weight (kg)	52.4 ± 5.5	54.7 ± 8.1	0.234
BMI (kg/m^2)	22.1 ± 2.7	24.5 ± 3.4	0.061
TGF-β1 (ng/mL)	8.1 ± 5.7	6.3 ± 3.6	0.027

Table 2. Relationship between age, height, weight or BML (x) and plasma TGF-β1 levels (y) in healthy controls.

x	y = plasma TGF-β1	Correlation coefficient
Age	y = −0.162x + 17.4	r = 0.197
Height	y = 0.658x − 92.5	r = 0.411
Weight	y = −0.374x + 28.4	r = 0.291
BMI	y = −0.982x + 30.6	r = 0.395

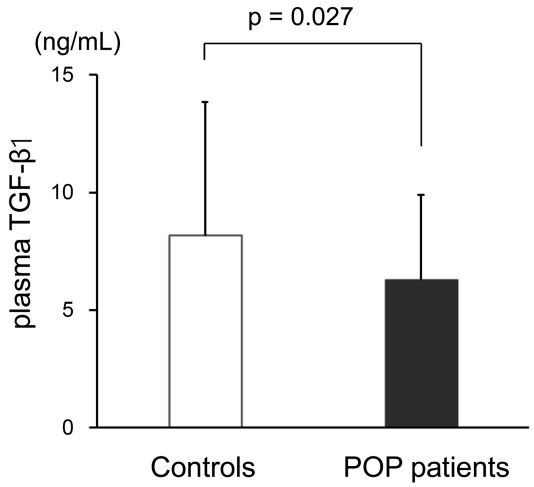

Figure 1. Comparison of plasma TGF-β1 levels between women with pelvic organ prolapse (POP, n = 49) and healthy control women (Controls, n = 23). Plasma TGF-β1 levels were significantly (p = 0.027) lower in POP patients (6.3 ± 3.6 ng/mL) than in healthy controls (8.1 ± 5.7 ng/mL) (Mean ± SD).

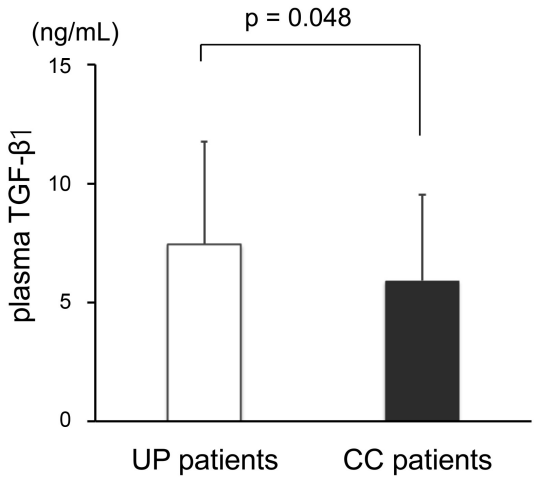

Figure 2. Comparison of plasma TGF-β1 levels between women with uterine prolapse (UP, n = 19) and those with a cystocele (CC, n = 30). Plasma TGF-β1 levels were significantly (p = 0.048) higher in the UP group (7.4 ± 4.3 ng/mL) than in the CC group (5.9 ± 3.6 ng/mL) (Mean ± SD).

Among the patients, 19 had UP and 30 CC. We found no significant differences in age, BMI, parity, and presence or absence of stress urinary incontinence between the two subgroups (**Table 3**). Although POP-Q stage was also not significantly different between the two subgroups, POP-Q stage IV was diagnosed in 63% of patients with UP but in only 7% of those with CC. Plasma TGF-β1 levels were significantly (p = 0.048) higher in the UP group (7.4 ± 4.3 ng/mL) than in the CC group (5.9 ± 3.6 ng/mL) (**Figure 2**).

Table 3. Basic characteristics of women with uterine prolapse (UP) and those with a cystocele (CC).

	UP patients (n = 19)	CC patients (n = 30)	p-value
Age (years old)	66.2 ± 7.4	66.3 ± 9.4	0.425
BMI (kg/m^2)	24.2 ± 3.4	25.3 ± 3.3	0.121
Parity (times)	3.6 ± 1.0	3.6 ± 1.0	0.389
POP-Q stage			
II	2 (11%)	4 (13%)	0.320
III	5 (26%)	24 (80%)	
IV	12 (63%)	2 (7%)	
Presence of stress urinary incontinence			
Yes	11 (58%)	13 (43%)	0.191
No	8 (42%)	17 (57%)	
TGF-β1 (ng/mL)	7.4 ± 4.3	5.9 ± 3.6	0.048

4. Discussion

The present study aimed to clarify whether plasma TGF-β1 levels are also decreased in POP patients, similar to TGF-β1 levels in POP tissues. Although the healthy controls were significantly younger than the patients, all participants were postmenopausal, and plasma TGF-β1 levels did not correlate with age, height, weight, or BMI in the healthy controls; consequently, it was determined that the healthy female volunteers were suitable as controls for patients [22]. Plasma TGF-β1 levels were significantly lower in patients than in healthy controls. This result is consistent with previous findings of reduced TGF-β1 expression in the pubovaginal fascia and cardinal ligament tissues of patients with POP [16]-[20]. Moreover, among the patients, plasma TGF-β1 levels were significantly lower in the CC group than in the UP group, indicating that plasma TGF-β1 levels might reflect TGF-β1 expression in the pelvis.

TGF-β1 is involved in the synthesis of the extracellular matrix and the inhibition of matrix metalloproteinases. Furthermore, sustained elevations of TGF-β1 have been associated with multiple other pathological conditions, such as pulmonary fibrosis, keloid formation, coronary artery restenosis, and acute respiratory distress syndrome [23]. Thus, although the molecular mechanism of TGF-β1 remains unclear, TGF-β1 expression is enhanced in conditions with increased fibrosis in tissue. Increased mechanical strain can reduce the expression of TGF-β1 [23] [24], so it is understandable that both collagen and TGF-β1 expression are reduced in POP tissues [10]. However, TGF-β1 expression was reported to be increased in the fascia of inguinal hernias [25] and POP tissues of higher stage POP (POP-Q stage IV) but not lower stage POP (POP-Q stages II and III) [22]. These

findings are interesting because both inguinal hernias and POP are associated with a loss of fascial support, so the pathophysiology of the two conditions might be similar [22]. In the present study, POP-Q stage IV was diagnosed in 63% of patients with UP and 7% of those with CC, and plasma TGF-β1 levels were significantly higher in the UP group than in the CC group; these results indicate that UP and CC may differ in the degree of TGF-β1 involvement in their disease progression.

Several diseases have been reported to be associated with elevated plasma TGF-β1, including schizophrenia [26], astrocytoma [27], open-angle glaucoma [28], advanced or metastatic cancers [29]-[33], chronic pancreatitis [34], atrial fibrillation [35] and hypertension [36] [37], and many of these diseases also show elevated TGF-β1 expression in the pathogenic tissues. However, we were unable to find any reports on diseases where plasma TGF-β1 is decreased, and the only study that found decreased plasma TGF-β1 was on physical exercise [38]. Hence, to the best of our knowledge this is the first report of a disease in which plasma TGF-β1 is decreased. The question whether decreased plasma TGF-β1 levels indicate a reduction in systemic TGF-β1 activity is unclear, but they can be assumed to reflect reduced TGF-β1 expression in POP tissues.

Angiotensin II subtypes 1 receptor antagonists and angiotensin-converting enzyme inhibitors inhibit TGF-β1 activity [36]. Tranilast, an anti-allergic agent and keloid treatment, also suppresses TGF-β1 activity [39]. Tranilast results in thinning of the bladder wall, causing interstitial cystitis-like symptoms [40]. Therefore, future studies may be able to evaluate whether these drugs affect the onset of POP by measuring plasma TGF-β1.

This study has some limitations. The number of controls was small, and age was significantly different between patients and controls, although all participants were postmenopausal. Future studies are needed to evaluate whether plasma TGF-β1 levels change with age. Moreover, because we did not compare TGF-β1 expression in POP tissues and plasma TGF-β1 levels, our findings are preliminary.

5. Conclusion

Plasma TGF-β1 levels are significantly lower in patients with POP than in healthy controls and significantly lower in patients with CC than in those with UP. It remains unclear whether the lower levels indicate a reduction in systemic TGF-β1 activity, but they can be assumed to reflect reduced TGF-β1 expression in POP tissues, especially in CC tissues. Future studies may be able to measure plasma TGF-β1 to investigate whether drugs affect connective tissue formation and the onset of POP.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

BMI: Body Mass Index;
CC: Cystocele;
POP: Pelvic organ Prolapse;
POP-Q: POP Quantification System;
SD: Standard Deviation;
TGF-β1: Transforming Growth Factor-Beta 1;
UP: Uterine Prolapsed.

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A Panorama of the Urological Diseases at the Former Military Teaching Hospital of Cotonou

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Abstract

Background: Urological care has been advancing quickly over the last ten years in Benin. In order to conveniently support that trend towards better urological care standards, decision-makers need sound data on urological diseases in the country. **Objective:** To determine the prevalence of urological diseases in the former Military Teaching Hospital of Cotonou. **Patients and Method:** We retrospectively collected the urological diseases that the institution had managed from January 2012 to December 2020. We used Excel© 2010 and SPSS© to analyze the collected data. **Results:** 4244 patients, *i.e.* 3717 males (87.58%) and 527 females (12.42%) were managed during the study period. The main diseases diagnosed were benign prostatic hyperplasia (32.61%, n = 1384), erectile dysfunction (10.44%, n = 443), chronic prostatitis (5.94%, n = 252), prostate cancer (4.03%, n = 171), and ejaculatory disorders (3.44%, n = 146). In patients ≤ 15 years, predominant diseases were peritoneal vaginal canal (15.9%, n = 43), circumcision (15.6%, n = 42), testicular dystopia (10.7%, n = 29), hydrocele (7.8%, n = 21), and hypospadias (5.6%, n = 15). Wilms tumor (1.9%, n = 5) was the first cancer, testicular (0.4%, n = 1) and para-testicular (0.4%, n = 1) tumors were the next. In patients > 15 and ≤40 years, the main diseases were infertility (14.1%, n = 189), chronic prostatitis (12.9%, n = 173), erectile dysfunction (10.1%, n = 135), ejaculatory disorders (6.2%, n = 83), genital infections (6.2%, n = 83) and urinary stone (4.9%, n = 66). The first cancer was kidney cancer (0.97%, n = 13) followed by bladder cancer (0.3%, n = 4) and testicular tumor (0.3%, n = 4). In patients >40 years, the most prevalent diseases were BPH (52.0%, n = 1370), erectile dysfunction (11.7%, n = 308), prostate cancer (6.5%, n = 171), inguinal hernia (5.1%, n = 134), and urinary stone (3.9%, n = 102). Prostate cancer is the first cancer; the next were bladder (0.95%, n = 25) and kidney (0.68%, n = 18) cancers. **Conclusion:** Benign prostatic hyperplasia and urological cancers (prostate, bladder

and kidney cancers) were the main urological diseases at the former Military Teaching Hospital of Cotonou. Urological malformations and Wilms tumor were the main diseases in the children.

Keywords

Urological Diseases, Former Military Teaching Hospital of Cotonou

1. Introduction

The former military teaching hospital of Cotonou settled its urological department in January 2012. It was the first military urological care unit and the second ever created in Benin. In 2013, the military teaching hospital of Cotonou was the first healthcare facility to introduce the TRUS-guided prostate biopsy in the country [1]. In 2014, the hospital performed its first radical prostatectomy and introduced in the country, the transurethral resection of prostate and bladder. In the same year 2014, the facility performed its first radical cystectomy. These last years, urological care has been both modernizing and extending to more and more geographical areas. To efficaciously further that trend, there is a need to characterize the epidemiology of urological diseases in the country. Evaluating the ten-year-long urological care of the former military teaching hospital of Cotonou can help to meet that need.

2. Objective

To determine the prevalence of urological diseases in the former Military Teaching Hospital of Cotonou.

3. Patients and Method

We retrospectively studied the diseases managed from January 2012 to December 2020 in the urological department of the former military teaching hospital of Cotonou. We collected the diseases, the number of cases of each disease and the demographic data of the affected patients. We excluded cases in which the diagnosis was unclear or non-urological or the cases in which the patient demographic data were not available. We analyzed the collected data by means of Excel© and SPSS©. We calculated the prevalence of each recorded disease in the whole population of patients. Then we studied the diseases and their prevalence in the children (patients aged 15 years or less), the young adults (aged from 15 to 40 years or less) and the adults (patients above 40 years old). In the patients older than 40 years, we further analyzed the disease prevalence through age subgroups and compared the prevalence of prominent diseases between those age subgroups. Doing so leads us to the results below.

4. Results

4244 patients were studied including 3717 males and 527 females. Among them

were 270 children (≤15 years old), 1341 young adults (aged 15 to 40 years) and 2633 adults (>40 years old). Their demographic data are exposed in Table 1.

The main diseases diagnosed in the patients were benign prostatic hyperplasia (32.61%, n = 1384), erectile dysfunction (10.44%, n = 443), chronic prostatitis (5.94%, n = 252), prostate cancer (4.03%, n = 171), ejaculatory disorders (3.44%, n = 146). The spectrum of urological disease observed varied from childhood to adulthood (Table 2).

Predominant diseases in patients aged 15 years or less were peritoneal vaginal canal (15.9%, n = 43), circumcision (15.6%, n = 42), testicular dystopia (10.7%, n = 29), hydrocele (7.8%, n = 21), hypospadias (5.6%, n = 15). The first cancer in the children was Wilms tumor (1.9%, n = 5). The other childhood tumors were testicular (0.4%, n = 1) and para-testicular (0.4%, n = 1) tumors.

In young adults, *i.e.* individuals 15 to 40 years old, the main diseases were infertility (14.1%, n = 189), chronic prostatitis (12.9%, n = 173), erectile dysfunction (10.1%, n = 135), ejaculatory disorders (6.2%, n = 83), genital infections (6.2%, n = 83) and urinary stone (4.9%, n = 66). The first cancer in that age group was kidney cancer (0.97%, n = 13) followed by bladder cancer (0.3%, n = 4) and testicular tumor (0.3%, n = 4).

In patients older than 40 years (Table 2 and Table 3), the most prevalent diseases were BPH (52.0%, n = 1370), erectile dysfunction (11.7%, n = 308), prostate cancer (6.5%, n = 171), inguinal hernia (5.1%, n = 134), urinary stone (3.9%, n = 102). Here, prostate cancer is the first cancer; the next cancers were bladder cancer (0.95%, n = 25), kidney cancer (0.68%, n = 18), adrenal tumor (0.19%, n =

Table 1. Demographic characteristics of the patients.

Patients	Sex		Total
	Male	Female	
Population			
Size n (%)	3717 (87.6)	527 (12.4)	4244
Number (%) of patients			
≤15 years	237 (87.8)	33 (12.2)	270 (6.4)
15 to 40 years	1142 (85.2)	199 (14.8)	1341 (31.6)
≥40 years	2338 (88.8)	295 (11.2)	2633 (62.0)
Age (years)			
Mean	47.4	43.3	46.9
Min.	0.5	1	0.3
Max.	102	95	102
Mean age of patients			
≤15 years	7.1	8.6	7.3
15 to 40 years	30.2	29.4	30.1
≥40 years	59.9	56.6	59.6

Table 2. Diseases and their prevalence in the whole population of patients.

AGE GROUPS (YEARS)					
AGE ≤ 15 YEARS (n = 270)		**15 < AGE ≤ 40 (n = 1341)**		**AGE > 40 (n = 2633)**	
DISEASES	**PREVALENCE % (n)**	**DISEASES**	**PREVALENCE % (n)**	**DISEASES**	**PREVALENCE % (n)**
Peritoneal-vaginal canal	15.93 (43)	Infertility	14.09 (189)	BPH	52.03 (1370)
Circumcision	15.56 (42)	Chronic prostatitis	12.9 (173)	Erectile dysfunction	11.7 (308)
Testicular dystopia	10.74 (29)	Erectile dysfunction	10.07 (135)	***Prostate cancer***	**6.49 (171)**
Hydrocele	7.78 (21)	Ejaculatory disorders	6.19 (83)	Inguinal hernia	5.09 (134)
Hypospadias	5.56 (15)	Genital infections	6.19 (83)	Urinary stone	3.87 (102)
Cystitis	2.96 (8)	Urinary stone	4.92 (66)	Renal cyst	3.84 (101)
Inguinal hernia	2.22 (6)	Varicocele	4.92 (66)	OAB	3.42 (90)
Enuresis	2.22 (6)	Cystitis	3.06 (41)	Chronic prostatitis	3.00 (79)
Wilms tumor	**1.85 (5)**	Inguinal hernia	2.61 (35)	DESD	2.96 (78)
Paraphimosis	1.85 (5)	Urethral stenosis	2.09 (28)	Infertility	2.66 (70)
Priapism	1.85 (5)	Hydrocele	1.86 (25)	Ejaculatory disorders	2.39 (63)
Testicular torsion	1.48 (4)	Venereal warts	1.79 (24)	Cystitis	2.2 (58)
Varicocele	1.11 (3)	OAB	1.57 (21)	Acute genital infection	2.16 (57)
Testicular agenesis	1.11 (3)	DESD	1.34 (18)	Obstructive renal failure	1.94 (51)
UPJO	1.11 (3)	BPH	1.04 (14)	Urethral stenosis	1.52 (40)
DESD	0.74 (2)	***Kidney cancer***	**0.97 (13)**	Hydrocele	1.48 (39)
Obstructive renal failure	0.74 (2)	Epididymal cyst	0.97 (13)	***Bladder cancer***	**0.95 (25)**
Spermatic cord cyst	0.74 (2)	Testicular dystopia	0.82 (11)	CKD	0.95 (25)
OAB	0.37 (1)	Renal cyst	0.74 (10)	***Kidney cancer***	**0.68 (18)**
Testicular tumor	**0.37 (1)**	Acute pyelonephritis	0.45 (6)	Varicocele	0.53 (14)
Para-testicular tumor	**0.37 (1)**	Testicular torsion	0.45 (6)	Acute pyelonephritis	0.3 (8)
Kidney trauma	0.37 (1)	Enuresis	0.37 (5)	Peyronie disease	0.3 (8)
Kidney ectopia	0.37 (1)	Priapism	0.37 (5)	POP	0.3 (8)
		Spermatic cord cyst	0.37 (5)	Epididymal cyst	0.27 (7)
		Ectopic kidney	0.37 (5)	***Adrenal tumor***	**0.19 (5)**
		Bladder cancer	**0.3 (4)**	UPJO	0.19 (5)
		Testicular tumor	**0.3 (4)**	Kidney ectopia	0.19 (5)
		CKD	0.3 (4)	***Testicular tumor***	**0.15 (4)**
		Testicular agenesia	0.3 (4)	Venereal warts	0.15 (4)

Continued

Ureteral stenosis	0.3 (4)	SUI	0.15 (4)
Peritoneal-vaginal canal	0.22 (3)	Breast cancer	0.11 (3)
Penile fracture	0.22 (3)	Vesical-vaginal fistula	0.11 (3)
UPJO	0.22 (3)	Acute renal failure	0.11 (3)
Circumcision	0.15 (2)	UG schistosomiasis	0.08 (2)
Para-testicular tumor	**0.15 (2)**	Priapism	0.08 (2)
Adrenal tumor	**0.07 (1)**	Penile fracture	0.08 (2)
UG schistosomiasis	0.07 (1)	Hypospadias	0.08 (2)
POP	0.07 (1)	Ureteral stenosis	0.08 (2)
Obstructive renal failure	0.07 (1)	Testicular torsion	0.04 (1)
Vesical-vaginal fistula	0.07 (1)	Testicular agenesis	0.04 (1)
Hypospadias	0.07 (1)	Spermatic cord cyst	0.04 (1)
Peyronie disease	0.07 (1)	Kidney trauma	0.04 (1)

5) and testicular tumor (0.15%, n = 4).

Below 60 years, the most prevalent diseases were BPH (40.9%, n = 588), erectile dysfunction (13.6%, n = 195), urinary stone (5.4%, n = 77), chronic prostatitis (5.1%, n = 74), inguinal hernia (4.1%, n = 59) and ejaculatory disorders (3.5%, n = 50). Prostate cancer (2.2%, n = 31), kidney cancer (0.7%, n = 10), bladder cancer (0.6%, n = 8) and testicular tumor (0.2%, n = 3) were the main cancers.

In 60 to 80 years old patients, BPH (65.9%, n = 729), prostate cancer (11.2%, n = 124), erectile dysfunction (10.0%, n = 111), inguinal hernia (6.2%, n = 69) and kidney cyst (5.7%, n = 63) were predominant. Prostate cancer (11.2%) was the first cancer tailgated by bladder (1.5%, n = 17) and kidney (0.7%, n = 8) cancers.

In patients above 80 years of age, the most prevalent diseases were BPH (59.3%, n = 53), prostate cancer (18.6%, n = 16), obstructive renal failure (9.3%, n = 8), inguinal hernia (7%, n = 6) and renal cyst (5.8%, n = 5). The only cancer in them was prostate cancer.

The difference in BPH prevalence was significant between the subgroups 60 to 80 years and 40 to 60 years ($p = 0.003$) and between the subgroups 80 to 100 years and 40 to 60 years ($p = 0.002$). The difference in prostate cancer prevalence was not significant between the subgroups 60 to 80 years and 80 to 100 years ($p = 0.12$).

5. Discussion

The collected data clearly drew a global epidemiologic picture of the diseases that were managed in the urological department of the hospital. In the whole

Table 3. Diseases and their prevalence in subgroups of patients >40 years of age.

AGE SUBGROUPS (YEARS)					
40 < AGE ≤ 60 (n = 1439)		**60 < AGE ≤ 80 (n = 1106)**		**80 < AGE ≤ 100 (n = 86)**	
DISEASES	**PREVALENCE % (n)**	**DISEASES**	**PREVALENCE % (n)**	**DISEASES**	**PREVALENCE % (n)**
BPH	40.9 (588)	BPH	65.9 (729)	BPH	59.3 (53)
Erectile dysfunction	13.6 (195)	***Prostate cancer***	**11.2 (124)**	***Prostate cancer***	**18.6 (16)**
Urinary stone	5.4 (77)	Erectile dysfunction	10.0 (111)	*Obstructive renal failure*	9.3 (8)
Chronic prostatitis	5.1 (74)	Inguinal hernia	6.2 (69)	*Inguinal hernia*	7 (6)
Infertility	4.5 (65)	Kidney cyst	5.7 (63)	Renal cyst	5.8 (5)
Inguinal hernia	4.1 (59)	OAB	3.6 (40)	DESD	4.7 (4)
Ejaculatory disorders	3.5 (50)	DESD	2.5 (28)	OAB	2.3 (2)
OAB	3.3 (48)	Urinary stone	2.2 (24)	Erectile dysfunction	2.3 (2)
DESD	3.2 (46)	Obstructive renal failure	2 (22)	Acute orchitis	2.3 (2)
Cystitis	2.6 (37)	Genital infection	1.9 (21)	POP	2.3 (2)
Genital infections	2.4 (34)	Cystitis	1.8 (20)	Anejaculation	2.3 (2)
Kidney cyst	2.3 (33)	Hydrocele	1.8 (20)	Urinary stone	1.2 (1)
Prostate cancer	2.2 (31)	***Bladder cancer***	**1.5 (17)**	Cystitis	1.2 (1)
Urethral stricture	1.5 (22)	Urethral stricture	1.5 (17)	Urethral stenosis	1.2 (1)
Obstructive renal failure	1.5 (21)	Ejaculatory disorders	1 (11)	Hydrocele	1.2 (1)
Hydrocele	1.3 (18)	CKD	1 (11)		
CKD	1 (14)	***Kidney cancer***	**0.7 (8)**		
Varicocele	0.8 (12)	Infertility	0.5 (5)		
Kidney cancer	0.7 (10)	Chronic prostatitis	0.5 (5)		
Bladder cancer	0.6 (8)	POP	0.4 (4)		
Acute pyelonephritis	0.4 (6)	Venereal warts	0.4 (4)		
Epididymal cyst	0.4 (6)	Acute pyelonephritis	0.2 (2)		
Peyronie disease	0.4 (6)	Varicocele	0.2 (2)		
Adrenal tumor	0.3 (4)	Acute renal failure	0.2 (2)		
UPJO	0.3 (4)	Peyronie disease	0.2 (2)		
Kidney ectopia	0.3 (4)	***Testicular tumor***	**0.1 (1)**		
Testicular tumor	0.2 (3)	***Adrenal tumor***	**0.1 (1)**		
SUI	0.2 (3)	***Male Breast cancer***	**0.1 (1)**		
UG schistosomiasis	0.1 (2)	Penile fracture	0.1 (1)		
POP	0.1 (2)	Vesical-vaginal fistula	0.1 (1)		

Continued

Priapism	0.1 (2)	UPJO	0.1 (1)
Vesical vaginal fistula	0.1 (2)	Epididymal cyst	0.1 (1)
Penile fracture	0.07 (1)	Hypospadias	0.1 (1)
Testicular torsion	0.07 (1)	SUI	0.1 (1)
Testicular agenesis	0.07 (1)	Kidney ectopia	0.1 (1)
Cyst of spermatic cord	0.07 (1)	Ureteral stricture	0.1 (1)
Kidney trauma	0.07 (1)		
Acute renal failure	0.07 (1)		
Hypospadias	0.07 (1)		
Ureteral stricture	0.07 (1)		

population of patients, the most prevalent urological diseases were prostate diseases, *i.e.* BPH, chronic prostatitis and prostate cancer, accounting for 42.6%. Next came erectile dysfunction (10.4%) and ejaculatory disorders (3.4%). The most prevalent cancer was prostate cancer (4.0%). Mungadi has also noticed that prostate diseases, *i.e.* BPH, prostate cancer and chronic prostatitis are predominant and make up 26.5% of all urological diseases [2]. Prostate cancer is the most common non-cutaneous cancer and the 2nd cause of cancer death in males [3] [4]. Nevertheless, the disease spectrum in our patients varied throughout their age groups.

In children, *i.e.* patients aged 15 years or less, malformations (peritoneal vaginal canal, testicular dystopia, hypospadias) were the main diseases (32.2%) and Wilms tumor, the first cancer (1.9%). Wilms tumor or nephroblastoma (7.5%), cryptorchidism (39.2%) and hypospadias (3.7%) are the main diseases in pediatric population [5].

In young adults (15 to 40 years old), the main issues were sexual and reproductive disorders (30.4%), chronic prostatitis and genital infections (19.1%) and urinary stone (4.9%). Cancers were rare (1.34%), the most prevalent was kidney cancer (0.97%). Lotti has noticed 12% of infertility, 8.9% to 68.7% of cases being associated with erectile dysfunction and premature ejaculation [6].

In adults (more than 40 years old), prostate diseases (*i.e.* BPH, prostate cancer and chronic prostatitis) were the most prevalent, accounting for 61.5%. Prostate cancer (6.5%) was on top of the cancers. Nevertheless, the disease prevalence was heterogeneous throughout subgroups of patients older than 40 years (**Table 3**). BPH prevalence was highest between 60 and 80 years. The difference in BPH prevalence was significant between the age subgroups 40 to 60 and 60 to 80 ($p = 0.003$) and between 40 to 60 and 80 to 100 years ($p = 0.002$). Prostate cancer prevalence increased from one age subgroup to the other although that increment was not significant between the age subgroups 60 to 80 and 80 to 100 years ($p = 0.12$).

6. Conclusion

Benign prostatic hyperplasia and urological cancers were the main urological diseases at the former Military Teaching Hospital of Cotonou. Urological malformations were the main disease in the children. The main malignancies in the adults were prostate, bladder and kidney cancers. The main malignancy in the children was Wilms tumor.

Limitations of the Study

This one-institution-based study of urological diseases might not reveal the actual prevalence of those diseases in the country's population. Still, the prevalence data obtained were sound as the patients managed in the Urological Department of the Former Military Teaching Hospital of Cotonou came from all parts of the Country.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Is Ultrasound the Urologist's Stethoscope in the Outpatient Clinic?

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Abstract

Ultrasound is a non-invasive diagnostic imaging modality that has become the urologist's stethoscope in the outpatient clinic for diagnosis and monitoring of various urological pathologies. **Objectives**: Check if office ultrasound is beneficial in the outpatient clinic, helpful in the management, affected by the economic crisis, and determine in which condition it is sufficient. **Materials and Methods**: Between 2012 and 2022, one thousand files were prospectively collected randomly. Many objectives were chosen to evaluate the impact of the economic crisis on the use of ultrasound, identify the clinical conditions where ultrasound is beneficial, determine the conditions where ultrasound was sufficient, and determine if ultrasound findings were helpful for management. **Results**: The economic crisis did not impact the use of ultrasound, when the chief complaint was flank pain, 56.7% had positive findings. In 54%, ultrasound was helpful to avoid the need for further imaging, and in 93.5%, ultrasound was helpful in the management of patients. When the chief complaint was LUTS, 25.6% had positive findings while 82.9% did not require further imaging, in 78.6%, ultrasound was helpful in the management. In the case of hematuria, 60.7% had positive findings, 20% did not need further imaging, and 81% of ultrasounds were helpful in the management. When patients present with urgency 31% had positive findings, 93.7% did not require more imaging and 76% of ultrasounds were helpful in management. In the case of dysuria as the chief complaint, 35.8% had positive findings, 77.7% did not need more imaging, and helpful in the management of 62.8%. **Conclusion**: Ultrasound is a valuable cost-effective tool in the outpatient clinic urology clinic for diagnosing and monitoring. It is safe, painless, and can be repeated easily which makes it the precious Urologist's stethoscope.

Keywords

Office Ultrasound, Hematuria, LUTS, Dysuria, Urgency

1. Introduction

Ultrasound (US) is a non-invasive diagnostic imaging modality that has become a reliable tool in the outpatient urology clinic for diagnosing and monitoring various urological conditions [1]. Compared to other imaging modalities, ultrasound has the advantage of being entirely safe, with no radiation exposure or need for contrast, making it a safer option for patients [2]. Additionally, it is a quick and painless exam, making it a preferred choice for patients, and can be repeated easily. With short training, urologists can achieve acceptable accuracy in identifying the most common pathologies scanned by ultrasound, helping them make a quick diagnosis and properly manage patients [3]. In addition, urologists can use ultrasound to follow up with their patients after management to check their post-void residue, degree of hydronephrosis after medical expulsive therapy, presence of fragments after ESWL or other invasive therapies, and recurrent bladder lesions after resection to determine management, such as cystoscopy or TURBT. This article explores the impact of the financial crisis as well on the use of ultrasound in the outpatient clinic.

2. Objectives

This study aims to evaluate the impact of the economic crisis on the use of ultrasound in outpatient clinics and has several objectives. Firstly, the study aims to assess how the economic crisis has affected the utilization of ultrasound in outpatient clinics. This will involve analyzing trends in the frequency of ultrasound usage and changes in the types of patients and clinical conditions for which ultrasound is ordered.

Secondly, the study aims to identify clinical conditions in outpatient clinics where ultrasound is particularly beneficial. Ultrasound can be used to monitor a wide range of conditions, including renal and bladder conditions and stone disease, regardless of the initial presentation.

Thirdly, the study aims to determine the conditions where ultrasound is a helpful management tool. By understanding which conditions benefit most from ultrasound-guided procedures, healthcare providers can improve the quality and safety of patient care.

Finally, the study aims to identify the conditions where ultrasound is sufficient as a diagnostic tool. This will help healthcare providers avoid unnecessary testing and reduce costs.

3. Materials and Methods

Between 2013 and 2022, we prospectively collected data from referrals to a single

center. One thousand files were randomly chosen by the secretary of the outpatient urology clinic and evaluated by the urologist and the chief resident of the department. These files were equally divided into two periods: before and after the economic crisis that began in September 2019 (Table 1). All of the ultrasounds were performed by one trained urologist using the Mindray equipped with two probes: 3.5 and 6 MHz. The kidneys and bladder were scanned in supine and oblique positions.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board at Sahel General Hospital, and the study was assigned the reference number 3/2022. All participants provided written informed consent prior to participation in the study.

4. Inclusion and Exclusion Criteria

Inclusion criteria were patients presenting with acute flank pain, gross hematuria, urinary storage symptoms, scrotal enlargement, UTI, LUTS, and urinary retention.

Exclusion criteria were patients presenting with muscular pain, UTI, ED, infertility, hypospadias, undescended testis, high PSA, varicocele, torsion-detorsion, and spermatocele.

Table 1. Patients characteristics with US.

Age	0 - 15 y	45
	16 - 30 y	95
	31 - 45 y	173
	41 - 60 y	168
	>60	177
Sex	Male:	417
	Female:	242
Co-morbidities	Total	322/659
	HTA	134
	D.M	84
	CAD	27
	Stone former	27
	Depression	19

5. Results

After excluding files that did not match the inclusion criteria, 695 patients underwent ultrasound in the urology outpatient clinic on their first visit. We ana-

lyzed multiple variables to answer the objectives mentioned above (Table 2).

5.1. Impact of the Economic Crisis

The impact of the economic crisis on the use of ultrasound before and after 2019 was not significant when comparing chief complaints. The use of ultrasound was similar between the two periods, with 316 and 343 ultrasounds performed after and before 2019, respectively.

5.2. Flank Pain

In an outpatient clinic, flank pain is commonly evaluated using ultrasound. This is because ultrasound is a noninvasive and inexpensive imaging modality that does not involve radiation exposure, can be repeated as needed, and can be used in emergency settings in case of flank pain [4]. In this study that included 266 patients with flank pain, 151 (56.7%) had positive ultrasound findings. In 54% of cases, ultrasound helped to avoid the need for further imaging, and in 93.5% of cases, ultrasound was helpful in the management of patients.

5.3. LUTS

LUTS is a common symptom that can be caused by various underlying conditions, such as Benign Prostate hyperplasia, urinary tract infections, bladder disorders, and other urological conditions [5]. In our study which included 117 patients with urinary LUTS, ultrasound was used to evaluate the diagnosis. 30 (25.6%) had positive ultrasound findings, while 97 (82.9%) did not require further imaging. Ultrasound was helpful in the management of 92 cases (78.6%).

5.4. Hematuria

Hematuria can be a symptom of various underlying conditions, such as infections, malignancy, kidney stones, and other urological conditions. Ultrasound is a non-invasive and safe imaging modality that can be used to evaluate the urinary tract and identify potential causes of hematuria. An accurate diagnosis of the underlying cause is essential in guiding appropriate treatment [6].

In our study, 79 patients presented with hematuria, and 48 (60.75%) had positive

Table 2. Results.

Chief complaint	Number	Positive findings	%	P-value	No need for more imaging	%	P-value	US Helpful in management	%	P-value
Flank	266	151	56.7	0.075	78	29.3	0.002	201	75.5	0.076
Hematuria	79	48	60.7	0.82	16	20	0.73	64	81	0.74
LUTS	117	30	25.6	0.059	97	82.9	0.002	92	78.6	0.173
Urgency	63	41	65.7	0.2	45	71.4	0.001	48	76	0.091
Dysuria	148	53	35.8	0.005	115	77.7	0.016	93	62.8	0.007

ultrasound findings. Ultrasound was helpful in directing the management of 64 cases (81%), while 16 (33%) did not require further imaging.

Out of 87 patients presenting with gross hematuria in our study, 20 were diagnosed with bladder tumors using the US (22.9%).

5.5. Urgency

Urgency, or the sudden need to urinate, is a common symptom that can be caused by various underlying conditions, such as urinary tract infections, overactive bladder syndrome, and interstitial cystitis. In our study that included patients with urgency as their initial presentation in a clinic, ultrasound was used to evaluate the frequency of positive findings. Of the 48 patients, 15 (31%) had positive ultrasound findings ($P = 0.29$), 45 (93.7%) did not require further imaging ($P < 0.001$), and ultrasound was helpful in the management of all cases (76%, $P = 0.09$).

5.6. Dysuria

Dysuria is a symptom that can be caused by various underlying conditions, such as urinary tract infections, sexually transmitted infections, bladder inflammation, interstitial cystitis, kidney or ureteral stones, and certain types of cancer. In our study which included 148 clinic patients with dysuria, ultrasound was used to evaluate the frequency of positive findings. Of the 148 patients, 53 (35.8%) had a positive ultrasound finding. In 77.7% of cases, further imaging was not necessary, and ultrasound was helpful in the management of 93 cases (62.8%). These findings suggest that ultrasound can be a valuable tool in managing dysuria, as it can potentially avoid the need for unnecessary imaging and aid in treatment decision-making.

6. Discussion

Office ultrasonography is an increasingly popular diagnostic imaging modality in urology clinics due to its numerous advantages even for children [7]. It is a non-invasive and painless option that allows for rapid and repeatable evaluation of urologic complaints, making it convenient for patients. Additionally, ultrasonography aids in prompt diagnosis, avoiding delays in treatment, and augmenting physical exams [1]. As a result, it has become the preferred diagnostic modality for many urologic emergencies, such as scrotal trauma [8].

Compared to CT or MRI, ultrasound is completely safe and does not expose patients to radiation or require contrast agents. This makes it a safer option for patients, particularly those presenting with signs of malignancy, such as hematuria, especially in the case of microscopic hematuria [9].

One of the objectives of our study was to evaluate the influence of the economic downturn on the utilization of ultrasound in the ambulatory urological setting and determine the clinical indications where ultrasound confers benefits.

Our findings indicate that the impact of the financial crisis on the use of ul-

trasound was not statistically significant, as the number of ultrasounds performed remained consistent between the two time periods. Specifically, 316 ultrasounds were conducted after 2019 compared to 343 ultrasounds before 2019, suggesting that ultrasound remains a prevalent, economical, and efficient diagnostic imaging modality in urology outpatient clinics. This is likely due to its non-invasiveness, which makes it the preferred modality regardless of patient age [10]. In addition, it has clearly reduced the number of clinical consultations and assisted in treatment planning.

Although subject to variability, urologists, including trainees, with short training can achieve acceptable accuracy in identifying the most common pathologies scanned by ultrasound, enabling them to quickly diagnose and properly manage patients [3].

The use of ultrasound in emergency departments has been shown to shorten the length of stay for patients presenting with flank pain [11]. In addition, Ultrasound can accurately detect hydronephrosis and kidney or urinary tract stones, as well as identify the location of stones in the UPJ and UVJ if the bladder is full, which can eliminate the need for further imaging, such as CT scans, thereby reducing radiation exposure, time, and cost [12]. In cases where acute flank pain is accompanied by hydronephrosis, medical expulsive therapy can be initiated, and the degree of hydronephrosis can be monitored throughout and after treatment, whether it is medical, ESWL, or surgical.

Our study revealed that urologists can use ultrasound in the majority of patients presenting with flank pain, and more than half of these patients had positive findings. Ultrasound was helpful in guiding the management of over 93% of patients, reducing the cost and the need for further visits when findings were normal.

Furthermore, ultrasound can detect other renal pathologies, including UPJ obstruction, kidney mass, angiomyolipoma, adrenal mass, and complex cysts.

Even though patients presenting with lower urinary tract symptoms (LUTSs) have low positive findings, ultrasound can still aid in the management of over 78% of patients when done in the outpatient clinic by a urologist, thereby avoiding the need for further imaging and reducing the risk of radiation exposure, cost, and follow-up visits.

In the case of benign prostatic hyperplasia (BPH) and LUTS, ultrasound can be used to assess intravesical prostatic protrusion (IPP) and Detrusor wall thickness, measure prostate volume, and detect the presence of diverticulae. Franco *et al*. found that these two parameters can accurately diagnose bladder prostatic obstruction (BPO) in patients with LUTS due to BPH [13], while Kalkani *et al*. showed that increased IPP values are associated with a lower response to alpha-receptor-specific management [14]. In addition, ultrasound can be used to measure the post-void residual urine volume (PVR) before prescribing anticholinergics and to assess the success of alpha-blockers in reducing this residual urine. However, some studies have found that ultrasound is not reliable for measuring

PVR compared to the volume of urine drained by a urethral catheter, as Abdel wahab *et al*. demonstrated in their prospective study on 45 men with LUTS/BPH [15].

For patients exhibiting the symptom of hematuria, there is a growing need for clinical ultrasound as a diagnostic modality. When examined fully, positive Rosenkilde *et al*. suggested the possibility of ultrasound to replace follow-up cystoscopy to check for recurrence and found that this can be used in low-grade tumors only and noted, when examined fully, findings indicating bladder tumors were present in more than half of the patients [16].

Most of our patients underwent further imaging, which is consistent with the findings of other authors. In Australia, Ooi *et al*. conducted a study on the role of proper assessment of patients using ultrasound on patients presenting for the first time with hematuria and demonstrated the efficiency in guiding the proper management and referral [6]. In the era of computed tomography urography (CTU), some authors evaluated the role of ultrasound in patients presenting with gross hematuria and concluded that the US adds little benefit in this setting and should not be used [17]. In evaluating the proper approach to patients with hematuria, Willis and Tewelde confirmed the superiority of CTU [18]. In a large study comparing renal and bladder ultrasound to CTU in patients presenting with microscopic hematuria at identifying urinary tract malignancy, Wei Shen Tan *et al*. concluded that the sensitivity of RBUS was lower than CTU for the detection of bladder cancer (both < 85%) and that cystoscopy has higher accuracy [19]. Smith *et al*. published their 20-year experience in a community hospital in the evaluation of asymptomatic hematuria by renal ultrasound to detect upper urinary tract malignancy. Ultrasound had 100% sensitivity in detecting renal cell carcinoma and upper tract urothelial malignancy. They concluded that Ultrasonography is an appropriate modality for upper tract imaging in the initial evaluation of patients with asymptomatic microscopic hematuria [20].

Ultrasound has changed our management regarding patients presenting with hematuria with a bladder tumor seen on ultrasound which has shifted our decision to perform direct TURBT instead of a previous diagnostic cystoscopy.

Dysuria is one of the primary chief complaints that prompt patients to seek consultation. It can be caused by various medical conditions, including urinary tract infection, interstitial cystitis, or bladder cancer. In this study, ultrasound was found to be helpful in managing dysuria in more than half of the cases.

Ultrasound goes beyond its primary function as a diagnostic tool, as it has also proven to be a valuable imaging technique for follow-up purposes. This includes patients who have a history of kidney stones, kidney cysts, or benign masses, as well as for post-treatment imaging after surgical or medical removal of stones. Ultrasound can be used alone or in conjunction with KUB [21] [22].

However, some limitations were noted in this study. Firstly, it is a retrospective study with prospectively collected data. Secondly, it was performed by a single trained urologist, and the results were not confirmed by another radiologist

or urologist. Thirdly, due to the economic crisis and COVID-19 lockdown, more than half of the patients did not show up for the follow-up, which can affect the results of positive findings, given that sonography has its inherent limitation as a sole test.

7. Conclusions

In conclusion, ultrasound is a valuable tool in the outpatient urology clinic for diagnosing and monitoring various urological conditions. It is a safe, quick, and painless exam that can be repeated easily, making it a preferred choice for patients and an Urologist's precious stethoscope.

We should remember that the ultrasound is a "double sword". Being operator dependent, the possibility of misdiagnosis is higher in non-well-trained physicians. Any suspicious finding(s) should be confirmed by an imaging, or another ultrasound performed by a certified radiologist.

Although further testing, such as computed tomography (CT) or magnetic resonance imaging (MRI), may be necessary to confirm the diagnosis and provide more detailed information about the extent and severity of the condition. Ultrasound has been able to answer urologists' on-spot questions regarding the future management of patients and thus can be considered an urologist stethoscope in the outpatient clinic.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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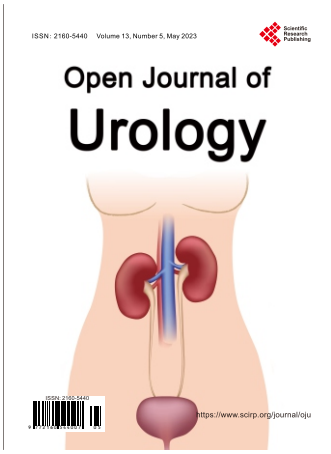

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