

## Research

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# Prevalence of Urogynaecological Symptoms in Survivors of Cervical Cancer in a Tertiary Care Gynaecologic Oncology Clinic of a Developing Country

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## ABSTRACT

**Background:** A lot of research has focussed on bowel symptoms but data is relatively scarce on exact burden of urinary subset of urogynaecological symptoms in survivors of cervical cancer.

**Aims and objectives:** To find out the prevalence of urinary subset of urogynaecological symptoms, in women with advanced cervical carcinoma treated with surgery and/or radiotherapy and comparing same with a control group.

**Methods:** A questionnaire incorporating demographic and urogynaecological (urinary) symptoms (IUGA terminology) was prepared and used to interview over 400 women between October 2008 and June 2010 in a case control observational design; 200 patients (study group) with history of treated cervical cancer, attending gynaecological cancer clinic and 200 patients (control group) with benign conditions attending Gynaecology outpatient clinic were interviewed. The frequency of various urinary problems was correlated with the demographic data and cystoscopic findings wherever appropriate and available.

**Results:** Increased daytime frequency of urination (25% vs. 6%, p=0.0001), dysuria (25% vs. 3%, p= 0.0001) and hematuria (26% vs. 2%, p= 0.0001) were seen more in cervical cancer patients compared to the controls. Nocturia (30% vs. 6%, p=0.6) and urinary hesitancy (7% vs. 2%, p=0.09) did not show any statistically significant difference. Among urinary incontinence, 'any' urinary incontinence (38% vs. 3%, p=0.0001), urge incontinence was seen in 1% vs. 3%, stress incontinence in 28% vs. 8%, p=0.0001, "continuous (extra urethral origin)" incontinence was seen in 8% vs. 0% and "mixed" incontinence in 1% vs. 2% (all cancer versus control group).

**Conclusions:** There is a high burden of urogynaecological problems in women with carcinoma cervix treated with surgery and/or chemo-radiotherapy as compared to controls.

**KEYWORDS:** Carcinoma cervix; Urogynaecological problems; Urinary incontinence.

**ABBREVIATIONS:** IUGA: International Urogynecological Association; ICS: International Continence Society; STROBE: Strengthening the Reporting of Observational studies in Epidemiology.

## INTRODUCTION

Treatment of gynaecological cancer has its own unique sets of associated short- and long-term complications and morbidities. There is a lot of data available on the prevalence of bowel symptoms in patients treated and followed up for cancer of the cervix.<sup>1,2</sup> These complications vary according to whether surgical or non-surgical treatment was used.<sup>2,3</sup> Radiation

changes tissue pliability and vascularity, the latter by obliterating the small blood vessels as well as mucositis. This leads to vaginal atrophy, enteritis and cystitis. Cystitis is seen usually as radiation doses approach 3000 cGy to the bladder.<sup>1-6</sup> This presents as accompanied by suprapubic tenderness, dysuria, urinary frequency and urgency Incontinence. As doses to the bladder approach more than 6000 cGy, acute hemorrhagic cystitis, chronic cystitis, fibrosis with decreased bladder capacity, and fistula formation may ensue.<sup>1-6</sup> The treatment of urinary incontinence in patients with prior radiation exposure and history of radical hysterectomy is particularly complicated especially for continuous incontinence of extraurethral origin *viz* fistula as surgical treatments can be compromised by the poor vascular supply to the tissues after radiation therapy.<sup>4-7</sup> Chemotherapy has widespread effects on various systems and specifically to lower urinary tract, can be a cause of haemorrhagic cystitis.<sup>2-4</sup> While assessing the need for specialist urogynaecological input in our patients, we noticed that contemporary literature available on morbidity burden of urinary symptoms is restricted only to very few specific conditions/complications. Surgery in the form of radical hysterectomy has its own set of complications such as reduced/absent bladder sensation and ureteric fistulae (and the same has been adequately explored by researchers.<sup>3,4</sup> Both Constipation and urinary dysfunction have been reported in earlier studies due to injury to the parasympathetic nerves during pelvic surgery.<sup>3,6-7</sup> Women with cervical cancer frequently develop symptoms like hematuria and/or overactive bladder resulting from various causes including cystitis due to both direct and indirect effects of cancer and its treatments. The major syndromes encountered in these women are increased susceptibility to infections due to both physical and immunologic effects of treatment, haemorrhagic cystitis caused by chemotherapeutic urothelial toxins and urinary problems caused by both acute and chronic effects of radiation therapy. Radical hysterectomy also shortens vagina and affects coital function.<sup>5</sup> The incidence of bladder sensory symptoms is one of the most common and debilitating long-term complications of radical pelvic surgery and/or radiation for the treatment of cervical cancer.<sup>4-6</sup> Surgery involves inherent surgical complications, both general and specific, the latter including conditions like reduced/absent bladder sensation and ureteric damage with radical hysterectomy.<sup>8</sup> The pathophysiology is believed to be related to the disruption of the innervation to the bladder during surgery and several groups advocate adoption of nerve sparing surgical techniques to avoid these.<sup>3-6</sup> The number of women who report urinary symptoms may be the 'tip of the iceberg', and while the absolute prevalence of symptoms may be of academic interest, its impact on quality life will determine the need for health care services, specifically for the urogynaecologic subspecialty in the multidisciplinary set up of a tertiary care gynaecological cancer clinic.

The present study was conducted to find out the prevalence of a specific subset of urogynaecological problems in women with carcinoma cervix treated with surgery and/or radiation therapy. Determining the burden of such problems can

be used to provide urogynaecological/continence services in the community.

## MATERIALS AND METHODS

This study is part of our larger project on prevalence of urinary and bowel morbidity in follow-up patients of gynaecologic malignancies approved by the Ethics Committee of the Hospital. In this present study, using a case-control observational design a total of 400 women 200 patients (study group) with history of cervical cancer, treated with surgery, chemotherapy, radiotherapy or varying combinations of same and attending a dedicated gynaecological cancer clinic and 200 patients (control group) with benign gynaecological conditions attending General Gynaecological outpatient clinic from October 2008 to June 2010 were randomly chosen and recruited using random number tables, and interrogated regarding various urinary problems following surgery and/or radio therapy as per the designed questionnaire. Both the clinics are part of a tertiary care research and referral hospital in urban northern India. A questionnaire to assess various urinary problems following surgery and/or radio therapy was specially designed to conduct the study in English and Hindi language versions and the same was used for interviewing the subjects after obtaining written informed consent. It included demographic data of the women like age, parity, socio-economic status, urinary symptoms. We adapted the questionnaire developed by Kelleher et al<sup>9</sup> from Kings College Hospital London to develop the present questionnaire suiting our local needs. The symptoms were then reclassified from the data accrued as per the current definitions issued by the International Urogynecological Association (IUGA)/International Continence Society (ICS) Joint Report on the Terminology for Female Pelvic Floor Dysfunction,<sup>10</sup> as these definitions came after the study was underway. The questionnaire elicited information on the increased daytime frequency (Complaint that micturition occurs more frequently during waking hours than previously deemed normal by the woman), nocturia (Complaint of interruption of sleep one or more times because of the need to micturate. Each void is preceded and followed by sleep), dysuria (burning micturition), urinary hesitancy (Complaint of a delay in initiating micturition), haematuria, urinary incontinence (Complaint of involuntary loss of urine). They were enquired about the stress incontinence (Complaint of involuntary loss of urine on effort or physical exertion), urgency incontinence (Complaint of involuntary loss of urine associated with urgency), both of them (mixed incontinence) and continuous incontinence (Complaint of continuous involuntary loss of urine).

A priori sample size was calculated. Using national and hospital estimates for cervical cancer, a sample size of 193 is required in each group for an intended power of 0.80 and alpha error of 0.05. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) recommendations for case-control observational studies have been followed as far as practicable. The frequency of various urinary problems was correlated

with the demographic data and cystoscopic findings wherever appropriate and available. Statistical analysis was performed using Statistical Package For Social Sciences 20.0.0 (SPSS Inc.) using Chi Square test and Fischer exact test taking P value <0.05 as significant. The study was adequately powered to tell the association between urinary symptoms and patient groups.

**RESULTS**

The demographic profile and general information of the respondents is shown in Table 1. At baseline, more women in the gynaecological cancer clinic group were post menopausal. The distribution of index conditions of patients recruited from the General gynaecological clinic as controls was: Fibroid uterus: 60(30%), Chronic cervicitis: 55(27.5%), Pelvic Inflammatory disease: 35(17.5%), Endometriosis: 25(12.5%), Prolapse uterus: 25(12.5%).

Characteristics	Cases (Gynaecological Cancer clinic) (n=200)	Control (General Gynaecological Clinic) (n=200)	Total (n=400)	P value
Age: Mean(yrs)	50.87(10.7)	48.7(10.7)	49.77	0.05
Range (yrs)	35-68	32-56	32-68	
Parity	4(2-8)	4(0-6)	3.9	0.13
<b>Education</b>				
Illiterate	48	38	86	0.22
Literate	152	162	314	
<b>Socio-economic status</b>				
Below poverty	18	14	32	0.307
Poor	38	28	66	
Middle class	114	98	212	
Upper Class	30	40	70	
Postmenopausal	122	20	142	0.001
Diabetes mellitus	38	26	64	0.102

Table 1: Demographic Characteristics of patients.

There is high overall prevalence of urinary symptoms in patients treated for cancer cervix (104 out of 200; 52%, CI=44.8-59.1) compared to benign conditions (50 out of 200, 25%, CI=19.2-31.2); p=< 0.001. Various urinary symptoms in women treated for cervical carcinoma and benign conditions are shown in Table 2.

Frequency of urination (25% vs. 6%, p=0.0001), Dysuria (25% vs. 3%, p= 0.0001) and Hematuria (26% vs. 2%, p= 0.0001) are the symptoms that are seen more in cervical cancer patients compared to the benign conditions. Nocturia (30% vs.

6%, p=0.6) and urinary hesitancy (7% vs. 2%, p=0.09) did not show any statistical significance between the study and the control groups. Although various types of urinary Incontinence are seen in both the groups (Table 3), Overall urinary incontinence (38% vs. 3%, p=0.0001) and specifically stress incontinence (28% vs. 8%, p= 0.0001) and continuous (extraurethral i.e. fistula) incontinence 16% versus 0% (p=0.007) were more commonly noted in cervical cancer group compared to controls.

Urinary symptoms	Cervical cancer (cases) patients n=200 (%)	General Gynaecology (control) patients n=200 (%)	P Value
Frequency of urination	50(25)	12(6)	0.0001*
Nocturia	60(30)	12(6)	0.623
Burning micturition	50(25)	6(3)	0.0001*
Urinary hesitancy	14(7)	4(2)	0.092
Hematuria	52(26)	4(2)	0.0001*

\*Statistically significant

Table 2: Comparison of urinary symptoms between Cases and Controls

	Cervical cancer (Cases) n=200 (%)	Benign conditions (Control) n=200 (%)	P value
<b>Urinary Incontinence</b>	76(38)	6(3)	0.0001*
Stress incontinence	56(28)	16(8)	0.0001*
Urge Incontinence	2(1)	6(3)	0.623
Mixed Incontinence	2(1)	4(2)	1.000
Continuous incontinence (fistula)	16(8)	0(0)	0.007

\*Statistically significant

Table 3: Urinary Incontinence in cervical cancer and benign conditions.

We retrospectively analysed the cystoscopic findings in all the cervical cancer patients prior to radiotherapy (Table 4). In 65% of cases, there was no positive finding and even post-radiotherapy, it did not correlate significantly with regard to symptoms. Mean time to onset of urinary symptoms from completion of cervical cancer treatment was 14.14 weeks.

Findings	Percentage
Normal	65
Cystitis	17.5
Bullous Oedema	10
Growth	7.5

Table 4: Cystoscopy findings (%) in patients with cervical cancer prior to radiotherapy.

**DISCUSSION**

The treatment of cervical cancer may be surgical or using chemotherapy or radiation or a combination of either depending mainly on the stage mainly and secondarily on behaviour of the disease and patient characteristics.

All modalities may lead to pelvic pain and altered self body image leading to sexual dysfunction.<sup>1-6,11</sup> Thus there myriad

of ways how treatment of cervical cancer affects woman's health and generates several subsets of symptoms including pelvic floor dysfunction/urogynaecological symptoms.<sup>5</sup> Yet it is surprising that often pelvic floor care givers such as urogynaecologists, physiotherapists and continence nurses are missing as regular components of the multidisciplinary fabric expected of a gynaecological cancer clinic setup especially in developing countries like India where emergency obstetrics and gynaecological cancer are priority areas and urogynaecology is yet to arrive as a separate subspecialty. Amongst urogynaecological symptoms, most of the studies from gynaecological cancer groups focus on bowel/faecal symptoms and some on sexual function.<sup>1-7,11</sup> The relative dearth of data regarding the set of lower urinary tract symptoms explored by us may also point towards lack of holistic approach towards gynaecological cancer patients in many set-ups and the fact that often these symptoms stay unattended unless adequately probed for and hence they continue to impair quality of life as these may be perceived both by the patients and care-givers as less important in the context of the primary condition, that is cervical cancer. Nonetheless they are widely prevalent as seen in our study and may be indirectly contributing to the low quality of life scores in cancer patients and addressing them may be a useful adjunctive tool to increase positive perception of gynaecological cancer treatment strategies.<sup>5,11</sup> In the study of the quality of life of cervical cancer survivors compared with the quality of life of a sample of the general Korean female population,<sup>5</sup> the survivors reported more impaired social functioning and, as in earlier studies more severe constipation and diarrhoea, urinary symptoms, and chronic leg lymphedema. More studies to explore this premise would be needed to make recommendations for care givers in such setting.<sup>5,11</sup> As more women survive gynecologic cancer, they will encounter the long-term effects of treatment on their pelvic floor function. It may be noted in our results that while the age was not statistically different in the cases and control groups, many more women in the cases group were post menopausal. This is because of treatment related menopause, whether surgical/radiation/chemotherapy/chemoradiation. The urinary symptoms may partly be contributed by the urogenital atrophy induced by the iatrogenic menopause over and above other direct and indirect effects on the local tissues.

While the overall prevalence of urinary incontinence symptoms in gynaecologic oncology patients<sup>12</sup> has been reported by Del Priore et al to be 60%, with 23% reporting severe symptoms, how these statistics compare to the prevalence of pelvic floor disorders experienced by woman without gynaecologic cancer remains to be described. The incidence of long-term bladder dysfunction was reported by Benedetti et al in a case-control study of 76 patients undergoing neoadjuvant chemotherapy and type 3-4 radical hysterectomy for the treatment of locally advanced cervical cancer.<sup>6</sup> Detailed urogynecologic assessments were higher than expected based on previous reports, at 76%; the main disturbances were detrusor over activity (21%), mixed urinary incontinence (24%), and de novo stress incontinence (21%). Despite these high rates of abnormal urodynamic func-

tions, only 20 patients (26%) complained of urinary symptoms (sensory loss, difficult micturition, severe urinary incontinence).<sup>6</sup> How these statistics compare to the prevalence of pelvic floor disorders experienced by woman without gynecologic cancer remains to be described. This is one novel aspect of our study where we have used a random and substantially large control group from general gynaecology clinic to assess the prevalence. In our study, urinary symptoms were experienced by 52 % of patients following radiotherapy with the mean period of 14.14 weeks which was similar to studies done by Covens et al (1993),<sup>13</sup> Anderson et al (1997),<sup>14</sup> Klee et al (2000),<sup>15</sup> and Zola et al (2000).<sup>16</sup>

## CONCLUSION

Our study confirms the high prevalence of urogynaecological problems in survivors of cervical cancer patients compared to controls.

**CONFLICT OF INTEREST:** None.

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