

Urinary Incontinence and Overactive Bladder

A Review

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Overactive bladder (OAB) and urinary incontinence (UI) are common symptoms in the adult population. In 2002, the International Continence Society provided new definitions for lower urinary tract dysfunction but the prevalence, incidence and remission estimates of OAB and UI (and its different types) vary considerably across studies. Methodological aspects, such as the sample selection and the mode of data collection, should be taken into account when comparing results.

While some risk factors are well established, others, mostly evaluated in cross-sectional studies, have not been consistently associated with the occurrence of the symptoms and some caution is necessary when attempting to define causal relations. More longitudinal data are needed to confirm findings from previous studies.

Urinary tract dysfunctions are highly prevalent conditions among men and women and they present an important economic burden to society. Despite an important negative impact in the quality of life, urinary symptoms are often under-diagnosed and under-treated.

Key-words: urinary incontinence; overactive bladder; epidemiology.

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Urinary incontinence and overactive bladder are common conditions in the adult population, with impact on physical, psychological and social well-being, and represent an important burden to the economy of health services. The assessment of the frequency of urinary incontinence and overactive bladder symptoms in specific settings and the extent to which they are diagnosed and treated are important issues to define priorities and sustain public health strategies oriented to the reduction of the human and economic burden of urinary dysfunctions.

1. DEFINITION OF URINARY INCONTINENCE AND OVERACTIVE BLADDER

In 2002, the International Continence Society (ICS) provided new definitions for lower urinary tract dysfunction to be compatible with the WHO ICDH-2 (International Classification of Functioning, Disability and Health) and the ICD10 (International Classification of Diseases) (1).

Urinary incontinence (UI) was defined as “the complaint of any involuntary leakage of urine”, removing from the original definition its classification as “a social and hygienic problem”, which could lead to different estimates due to its subjective aspect. The definition of stress urinary incontinence was also revised to “the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing”. Urge urinary incontinence is classified as “the complaint of involuntary leakage accompanied by or immediately

proceeded by urgency” and mixed urinary incontinence as “the complaint of involuntary leakage associated with urgency and also with exertion, or on sneezing or coughing”. Overactive bladder (OAB) was equated with the urge syndrome and the urgency-frequency syndrome and defined differently than before. It is classified as “urgency, with or without urge incontinence, usually with frequency and nocturia, in the absence of infection or other proven aetiology”. Increased daytime frequency of voiding is “the complaint by the patient who considers that he/she voids too often by day”; nocturia “the complaint that the individual has to wake at night one or more times to void” and urgency is “the complaint of a sudden compelling desire to pass urine which is difficult to defer” (1).

Although individuals with urge and mixed urinary incontinence may be classified as having overactive bladder (“wet OAB”), a great proportion of the subjects experiences urgency and frequency without incontinence episodes (“dry OAB”) (2).

2. FREQUENCY AND RISK FACTORS

Urinary incontinence and overactive bladder are common symptoms among the adult population worldwide, affecting approximately 200 million people (3). Nevertheless, and although several studies were conducted to assess the prevalence of urinary symptoms, the estimates differ considerably across studies and settings (4-13).

Differences in the populations evaluated (e.g.: general population, pregnant women, elderly), survey methodology (e.g.: telephone, mail or personal interviews), and classification of the outcome (e.g.: "any urine leakage in the previous month", "any urine leakage in the last year") contribute to the difficulties in summarizing the available evidence on this topic (11).

Urinary incontinence has a different pathophysiology in women and men, which is reflected in the gender differences in the prevalence of its different types, age distribution and risk factors. Each of these conditions is described below, in terms of its frequency and risk factors, separately for women and men.

2.1. Overactive bladder

At the end of the last century no large population-based studies had been conducted to assess the frequency of overactive bladder symptoms (14). Epidemiologic evidence was predominantly focused on urge incontinence and did not consider common symptoms as frequency and urgency (4,8,14).

The NOBLE (National Overactive Bladder Evaluation) study, conducted in adult population aged ≥ 18 years in the United States, reported that 16.9% of women and 16.0% of men had overactive bladder symptoms 6. In Europe, the EPIC study (Sweden, Italy, Canada, Germany and United Kingdom) was the first large investigation assessing the lower urinary tract symptoms based on the new ICS definition, in a population aged above 17 years. The prevalence of overactive bladder was 13% in women and 11% in men (9). While the overall prevalence is similar in both sexes, there are gender differences in the age-specific estimates and regarding the predominant symptoms. It has been reported that women present higher prevalence before their sixties, whereas the prevalence after this age is lower than in men 6, 9, 14, 15. Overactive bladder with incontinence is the most prevalent type in women while overactive bladder without incontinence predominates among men 4.

2.2. Urinary incontinence

2.2.1. Women

Overall prevalence

In the general population, estimates based on definitions with great period frames for the report of urinary incontinence episodes (e.g.: "ever", "in the past 12 months") range from 5% in women aged 15 years or more to 69% in those over 18 years, with most studies providing estimates between 25% and 45% (11). In a systematic review published in 2003, the median prevalence of urinary incontinence among women was 27.6% (range: 4.8-58.4%) (7). A study in women over 17 years in four European countries, which defined urinary incontinence as any leakage or involuntary loss of urine during the preceding 30 days, presented prevalence estimates varying

from 23% in Spain to 44% in France 10. The most recent cross-national study on urinary dysfunction (EPIC study: Canada, Germany, Italy, Sweden and United Kingdom) reported that the proportion of incontinent adult women (≥ 18 years) was 18%, and only in Sweden the prevalence was above 20% (9).

Two distinct patterns have been described by different authors for the age distribution of urinary incontinence, regardless of its type: 1) an increasing trend with age and the highest prevalence among older women; 2) highest prevalence in the middle aged women (around menopause), with a slight decrease up to the seventies and rising again in older ages (13,16). The review referred above shows the latter pattern when analysing prevalence estimates for any or occasional (ever or in the past 12 months) urinary incontinence, whereas a steady increase up to the eighties when considering significant or regular (moderate and severe incontinence on severity index) incontinence (7).

Incontinence type

Several studies do not distinguish the incontinence types and therefore the knowledge on this topic is limited (17). Even so, the literature providing information regarding specific types of urinary incontinence in women is consensual and refers stress incontinence as the most prevalent, followed by mixed and urge types (7,11,17-19). Minassian et al. (7) reported a mean prevalence of 50%, 32% and 14%, respectively. However, this distribution is observed among young and middle-aged women. After their forties, stress incontinence tends to decrease and the mixed and urge types to increase (7,14,16).

The interpretation of the findings referring to different types of urinary incontinence should be cautious, considering that the ICS definitions are symptom-oriented. To determine the physiopathology of the reported symptoms (sphincteric insufficiency for stress type and detrusor overactivity for urge type) a clinical and/or urodynamic assessment would be necessary. Sandvik et al. (20) assessed the validity of the questions used in surveys in comparison with gynaecologist's diagnosis after urodynamic evaluation. The proportion of stress incontinence increased (from 51% to 77%) and the mixed type decreased (from 39% to 11%), while the proportion of the urge type remained similar (10% vs. 12%). Therefore, the most frequent error when using a symptom-based questionnaire is expected to be a misclassification of stress urinary incontinence as being of the mixed form.

Severity of urinary incontinence

Severity may be measured as the frequency of urine leakage or, more accurately, using a severity index. The Sandvik's Severity index (validated using a 48-hour pad weighing test) combines information about frequency (four levels: less than once a month; a few times a month; a few times a week; every day and/or night) and the amount of leakage (three levels: drops; small splashes; more than

small splashes). The index value obtained by the product of the frequency by the amount of leakage is categorized in four classes: mild, moderate, severe and very severe (if the amount is measured using the categories “drops” and “more than drops”, it is obtained a three level index: slight, moderate, severe) (21).

In Norway, the EPICONT study showed that, in women over 19 years, the prevalence of urinary incontinence (regardless of the frequency of urine losses) was 25% while 7% reported severe or daily episodes (13).

Severity is known to be related to increasing age and is associated with a decrease in quality of life (7). Some studies refer that severe cases seek for medical help more frequently (7,12,22,23). Minassian et al. (24) studied the variation in prevalence of urinary incontinence and risk factors given different definitions, showing that the magnitude of the association between known risk factors and severe urinary incontinence was stronger than observed for the mild forms of incontinence, suggesting that the latter may represent transient or non-pathologic states that might not be clinically relevant.

Incidence and remission

Data on the incidence and remission of urinary incontinence is scarce. In 2005, the epidemiology chapter of the International Continence Society report presented an average annual cumulative incidence ranging from 1% to 3% in women aged less than 60 years and from 5% up to 11% in older women (11). In a review published in 2008, considering studies published after 1980, reporting Australian data on prevalence and/or incidence in women, only two studies presented incidence estimates (25). Liu and Andrews (26) followed elderly participants for 2 years and the annual incidence for stress and urge type of urinary incontinence was, respectively, 16.5% and 22.6% when considering episodes occurring “at least occasionally”, and 1.6% and 2.1% when considering episodes occurring “often”.

In the Study of Women’s Health Across the Nation, American women aged 40-55 years were followed during 5 years and the average 1-year cumulative incidence of at least monthly incontinent cases was 11% per year (27).

In the United Kingdom, 79710 women were evaluated at home and, at the baseline, 34.2% were classified as incontinent (1-year period prevalence). Among these women, 25.2% were not incontinent in the follow-up (1-year remission period). The annual cumulative incidence was 8.8% (28).

In Norway, 489 women aged 50-74 years were evaluated during one year. no cases of spontaneous remission were reported and the cumulative incidence was 0.6%, corresponding only to 3 new cases. The low estimate may be explained by the fact that incidence estimates are vulnerable to stochastic variation when the number of new cases is small (29).

Risk factors

Several epidemiologic studies evaluated factors associated with the occurrence of urinary incontinence. While some determinants are well established, such as age, obesity, parity or hysterectomy, others, mostly evaluated in cross-sectional studies, have not been consistently associated with the occurrence of urinary incontinence and some caution is necessary when attempting to define causal relations (7,12).

It is well recognized that urinary incontinence is correlated with age (7,11), following one of the two patterns described above (13,16). While some authors report that age is positively associated with urge and stress urinary incontinence, others did not confirm the latter association (11).

Obesity has been established as a strong risk factor for stress and mixed incontinence and a weaker association was observed with urge incontinence and overactive bladder (12,30,31). A recent systematic review assessing the role of overweight and obesity on urinary incontinence reports strong evidence that, in addition to body mass index, waist-hip ratio and thus abdominal obesity may be an independent risk factor for incontinence in women (32).

Pregnancy is also associated with the occurrence of urinary incontinence (16). Although in many women the urinary incontinence is self-limited to pregnancy, those developing incontinence during pregnancy have a higher predisposition to have the symptoms later in life (11,33,34). It is still questionable if pregnancy is an independent risk factor for urinary incontinence or if the symptoms are attributable to childbirth mechanisms. Parity is known to increase the risk of urinary incontinence, although the magnitude of this association diminishes with age (16). Some studies refer that after one delivery there is little or no additional risk, while others suggest an increasing risk with increasing parity (11). Minassian et al. (7) showed that most studies reported parity as a risk factor, although they did not report on the effect of peripartum parameters, including the mode of delivery, that could have an influence on the development of urinary incontinence. Delivery is recognised as a determinant of stress urinary incontinence in women (11). Rortveit et al. (35), in a study of 15307 Norwegian women under 65 years, reported that women with previous caesarean section were at increased risk of stress and mixed urinary incontinence, when compared with the nulliparous, and women with a vaginal delivery were at greater risk compared to those who undergone caesarean. A possible protective effect of caesarean was reviewed by Nygaard (36) who reported that the protection conferred by this mode of delivery compared to vaginal childbirth may be dissipated after further deliveries and decreases with age. It is also pointed out the inconsistency in literature regarding the risk of incontinence according to the moment of the caesarean: if before or on labour.

The hormonal changes induced during peri- and

post-menopausal periods may increase the susceptibility to urinary infections and can cause storage symptoms (urinary urgency and frequency). Some authors report that post-menopausal women are more likely to have severe incontinence while others did not find differences between premenopausal and postmenopausal groups or describe a lower prevalence of urinary incontinence in the latter, although only for stress type and not for urge incontinence (7,11,37). Oestrogen therapy is one of the treatment options for stress urinary incontinence (38), although a recent review did not find evidence of a benefit of oestrogen replacement therapy (39). One controlled multicentric study revealed that after 4 years of treatment with a combination of oestrogen and progesterone, and independent of the age of the women, the risk of urge and stress urinary incontinence (40) and the severity of the incontinence actually increased (41).

Also regarding hysterectomy, the findings are inconsistent and its role remains controversial (11,42). Although most authors tend to support that hysterectomy increases the risk of urinary incontinence, others found no differences or a negative association between this procedure and incontinence (11,42-46).

Diabetes has been reported to increase the risk of urinary incontinence (47) and the National Health and Nutrition Examination Survey found that two microvascular complications caused by diabetes, macroalbuminuria and peripheral neuropathic pain, were associated with incontinence (48).

Functional (e.g.: mobility limitations, impaired vision) and cognitive (e.g.: dementia or lack of mental orientation) impairment was also shown to increase the risk of urinary incontinence (11,34). Constipation, smoking, family history and genitourinary prolapse have been studied as possible risk factors for urinary incontinence in women, but the findings are inconclusive (49).

2.2.2. Men

Prevalence, incidence and type

The epidemiology of urinary incontinence in men has not been investigated to the same extent as for females. Before 2002, the overall prevalence ranged from 3% to 11% (12). The systematic review published by Minassian et al. (7), in 2003, showed that the median prevalence of urinary incontinence among men was 10.5%, ranging from 1 to 34.1%. After the ICS new definitions and recommendations in 2002, the number of population based studies increased, and most reported lower prevalence estimates in men compared to women (11).

The UrEpik study evaluated almost 5000 men aged 40-79 years in four countries [Netherlands (Boxmeer); France (Auxerre); United Kingdom (Birmingham) and Korea (Seoul)]. Self-reported urine leakage varied from 7.1% (Korea) to 14.8% (United Kingdom) (50). Diokno et al. (51) described, among 21590 American men aged 18 or more years, a 12.7% prevalence of an episode of urinary incontinence (any type) in the previous month. Urge incontinence was the most prevalent type (45% of

all cases) except among participants with 18-35 years who reported a higher proportion of stress incontinence. In the EPIC study, the overall prevalence was 5.4% and, as in the previous American study, urge incontinence was the predominant type (overall prevalence: 1.2%; stress and mixed type: 0.6% each) (9).

Up to now the literature is consensual describing a steady increase of the urge type incontinence with increasing age, which is the major contributor to the overall increase in the frequency of urinary incontinence with age in men. Mixed urinary incontinence also tends to increase with age, while stress incontinence decreases after the forties (9,11,51).

Incidence data among men is even scarcer than for women. McGrother et al. (28) presented 39.6% as the 1-year remission proportion (baseline prevalence 14.2%) and, for the same time period, a cumulative incidence of 3.8%. In Australia, men aged 65 or more years were followed during 2 years. The incidence considering episodes occurring "at least occasionally" was 11.9% for stress incontinence and 17.4% for urge incontinence. For the "often" episodes it was, respectively, 2.2% and 3.4% (26).

Risk factors

Usually urinary incontinence in men is not an isolated problem and exists with other co-morbidities, such as urogenital symptoms or erectile dysfunction (11). Increasing age is associated with a higher proportion of incontinent cases (5,12,52) and other urinary symptoms, namely those related to overactive bladder (e.g.: urgency, nocturia) or urinary tract infections showed to be strongly associated with urinary incontinence in men (5,12).

Prostatectomy, especially radical prostatectomy, is well established as a risk factor for urinary incontinence in men and the risk seems to increase with the increasing age at time of surgery (11,34). As for women, partial or total immobilization is described to be related with an increase of urinary incontinence, especially among the elderly. Also men having neurological disorders, such as Parkinson, and those who suffered a stroke are more likely to develop incontinence (11).

3. MANAGEMENT OF URINARY SYMPTOMS

3.1. Awareness and help-seeking behaviour

Urinary incontinence and overactive bladder have an important negative impact in the quality of life (QoL), regarding physical, social, psychological, sexual well-being and daily activities (53). Even so, urinary symptoms are often under-diagnosed and under-treated (10,50,54,55.)

Studies on care seeking behaviours are consensual on the reasons for not getting professional care. Generally, the fact that urinary incontinence is disregarded as a serious problem and seen as part of the normal ageing process, the low expectations of a possible effective treatment, and

the embarrassment or fear of exposing this situation to health professionals may lead to low consultation rates and a low proportion of diagnosed patients (7,12,23,56). The report of the symptoms to health professionals is associated with its increasing severity and/or its impact on quality of life (12,22,23,28,50,57).

McGrother et al. (28) reported a similar proportion of men and women having a medical consultation due to abnormal urinary storage symptoms (12% and 13%, respectively). Independently of quality of life, men (aware of the context of prostate cancer) and older participants were more likely to seek for help (28). In the UrEpik study, among men with urine leakage, 25.6% of the European participants and only 9.0% of the men in Seoul consulted a doctor (50). Hunskaar et al. (10) reported that in incontinent women, the proportion of those having medical consultations varied from 16% in Spain to 36% among the German patients.

3.2. Treatment and costs

The costs of urinary incontinence and overactive bladder are related to diagnosis, treatment, use of pads, routine care, co-morbidities or loss of productivity (58), but most of the economic burden is underestimated considering the low proportion of incontinent subjects having medical consultations for that reason (59).

In 2000, the total cost of overactive bladder to health care systems (drug use, medical visits, co-morbidities, pads use) in five countries (Germany, Italy, Spain, Sweden and United Kingdom) was estimated to be 4.2 billion Euros and it was expected to increase to 5.2 billion in 2020 (59). PURE (Prospective urinary incontinence research), a non-interventional study of women seeking treatment for urinary incontinence in an outpatient setting, showed a mean total urinary incontinence annual costs ranging from 359€ in the UK/Ireland patients to 655€ in Spain, and personal costs vary according the country health care system, namely on reimbursement policies (60).

The management and costs of urinary symptoms vary among incontinent patients. Half of European women reporting urine leakage referred the use of pads, 5% were taking drugs and 5% had surgery for urinary incontinence problems (10). In the United States, from 13% of men with urine leakage episodes, 47% consulted a physician and 30% of those were taking prescription medicines, 18% underwent some kind of surgery and 4% were using a catheter (51).

So, it is not surprising that most economic expenditure may be attributable to the use of pads, surgical procedures, and pharmacological treatments. Conservative treatments (e.g.: pelvic floor exercises, bladder training, etc.) are usually attributed a lower economic burden (60).

Treatment options for patients suffering of urinary incontinence differ according the physiopathology of in-

continence. While urge incontinence responds to pelvic floor muscle treatment and anticholinergic medication, for stress incontinence the pharmacologic approach may not have the same impact (54). It is suggested that pelvic muscle training should be included in first-line conservative management programs for both urge and stress incontinence. Individuals with urge incontinence or overactive bladder should also adopt other behavioural changes, such as fluid management or scheduled voiding intervals (49,61). The guidelines on urinary incontinence from the European Association of Urology recommend lifestyle interventions and pelvic floor muscle training or bladder retraining as the initial management of urinary incontinence for men and women (62).

The pharmacological approach is common in overactive bladder / urge incontinence and the efficacy of anticholinergic drugs, which suppress bladder contractions, is well established (63). The most frequently used drugs are oxybutynin, trospium and propiverine (63-66) although some authors refer their adverse effects (e.g.: dry mouth, constipation) as possible reasons for discontinuation (49). Of late more recently developed molecules such as solifenacin and darifenacin, which specifically block the M3 muscarinic receptors, are also available. These new drugs might have some advantage in achieving clinical results with fewer side effects. However patients' response to treatment varies individually and some can respond well to one anti muscarinic and not to another despite molecular composition (67). Cystoscopic injection of botulinum toxin in the detrusor muscle has been studied and is a promising alternative for urge incontinence refractory to other pharmacological treatments (68,69).

The absence of effective and well tolerated pharmacological treatments for stress urinary incontinence limits the choices (70). The pharmacotherapy approach before surgical procedures includes alfa-adrenergic drugs, tricyclic antidepressants such as imipramine, and oestrogen (70), although the evidence for the latter is not consensual (40,41). Duloxetine, a serotonin and noradrenaline reuptake inhibitor, is in phase III controlled trials and it is suggested that can significantly improve the quality of life of women with stress urinary incontinence (71).

Surgery is used especially for stress urinary incontinence and it is rarely indicated for urge incontinence (49). Even so, it seems that electrical stimulation and sacral neuromodulation improve urge urinary incontinence and are recommended (34,62). The most frequent surgical procedures for stress incontinence are sling procedures and colposuspension in women or artificial sphincter in men (49,62).

Meanwhile, surgeries for stress incontinence, as vaginal tapes or sling procedures have been associated with a growing number of individuals with suboptimal results and there are few studies providing non-surgical treatment options for women with failed surgeries (72). However "re-do" surgery seems to meet with some measure of success (73).

4. METHODOLOGICAL ISSUES

The wide regional variation in the frequency of urinary symptoms reflects the methodological heterogeneity across studies, as well as cultural differences. In addition to subject-specific issues, such as the selected sex and age groups, the methods used to select and evaluate the participants are important issues in population-based surveys (74).

The assessment of urinary dysfunctions using questionnaires instead of clinical or urogynaecologic evaluations may contribute to an overestimation of mixed urinary incontinence and underestimation of the frequency of the stress type, as referred by Sandvik et al. (20). Kirschner-hermanns et al. (75) showed a poor correlation between the assessment of urinary incontinence using questionnaires and video urodynamic testing in adults aged 65 or more years. Although urodynamics may be more precise, it is an invasive method of evaluating urinary dysfunction and in a clinical basis, individuals who respond satisfactorily to conservative care have no need for urodynamic studies (76). Additionally, in epidemiological research, it would be too expensive to carry out studies of thousands of participants across wide geographical areas not using questionnaires as the assessment tool for urinary symptoms. Therefore, the International Consultation on Incontinence Questionnaire (ICIQ) develops valid instruments universally applicable both in clinical practice and research (77). The European Association of Urology recommends the ICIQ-SF, a questionnaire on symptom scores and quality of life (62).

The methods of questionnaire administration may also influence data quality, namely regarding sensitive questions as may be urinary topics.

When analysing the accuracy of survey reports about sensitive questions (e.g. illicit drug use, sexual behaviour or abortion), Tourangeau and Yan (78) showed that most studies comparing modes of data collection on these topics presented higher prevalence estimates on self-administered questionnaires than when questions were administered by an interviewer. Rhodes et al. (79) compared the effect of modes of administration (self-administered questionnaires, oral face-to-face in-clinic interview, and telephone interview) on responses to the American Urological Association Symptom Index among men. The report of urinary symptoms was generally higher in self-completed questionnaires when compared with clinical evaluations (face-to-face) and also higher than in telephone interviews, partly because of the possible embarrassment when reporting to an interviewer. Nevertheless self-administered questionnaires may result in suboptimal completeness and accuracy of data (e.g. comprehension difficulties among less educated participants, more neutral responses, as the "I don't know" options) which may reduce its validity (80).

Telephone surveys are an attractive option to collect health related data and may be a good cost-effective

strategy, providing accurate estimates on urinary symptoms (or, at least, underestimate the true prevalence, as referred above) as regarding several other health issues (6,9,14,81,82).

Allowing the coverage of large populations over wide geographical areas with a reasonable efficiency, these surveys are widely used and the selection of participants is frequently done using random-digit dialling or list-assisted frames schemes (83). The sampling strategy is also an issue of main importance in the survey design considering the increasing trends in non-coverage and non-response rates and what may be the effect of these problems on the validity of the estimates produced (84).

CONCLUSIONS

Urinary tract dysfunctions are highly prevalent conditions among men and women and with a wide geographic distribution. They present an important economic burden to society. Several risk factors are described, especially for women, but more longitudinal data are needed to confirm findings from previous studies and also to provide more information on incidence and remission rates.

Despite its impact on quality of life and the available treatment options, a minority of patients seeks for help and so, a low proportion is treated.

Estimates on prevalence and incidence of these diseases vary considerably across studies. Therefore, methodological aspects, such as the sample selection and the mode of data collection, should be taken into account when comparing results.

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