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Author: Gita D. Mishra Megan S. Barker Gerrie-Cor Herber-Gast Tim Hillard

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Highlights (for review)

Findings from this study suggest that depression is associated with the development of urinary incontinence symptom. It has a significant public health implication for the prevention and treatment of urinary incontinence. For instance when women in their twenty or thirties, seek advice or treatment on their UI symptoms, health professions should consider the possibility that depression and a history of depression may play a role in development of the condition

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Depression and the incidence of urinary incontinence symptoms among young women:

results from a prospective cohort study

Gita D. Mishra[a], Megan S. Barker[a], Gerrie-Cor Herber-Gast[a], Tim Hillard[b]

[a] Center for Longitudinal and Life Course research, School of Public Health, The University of Queensland, QLD, Australia

[b] Department of Obstetrics and Gynaecology, Poole Hospital NHS Trust, Poole, UK

Correspondence: Professor Gita Mishra

Center for Longitudinal and Life Course research, School of Public Health, The University of Queensland, QLD, Australia

Email: g.mishra@uq.edu.au

Telephone: +61 7 3346 5224

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ABSTRACT

Objective: To examine the association of depressive symptoms with subsequent urinary incontinence (UI) symptoms among young women.

Subjects and Methods:

Data were from a cohort of 5391 young women (born 1973-78) from the Australian Longitudinal Study on Women's Health. Generalised Estimating Equations (GEEs) were used to link depressive symptoms, and history of doctor diagnosed depression at Survey 2 (S2) in 2000 with the incidence of UI symptoms in subsequent surveys (from S3 in 2003 to S6 in 2012).

Results: 24% of women reported the incidence of UI over the nine-year study period, while the prevalence rose over time from 6.8% (at S2, aged 22-27 years) to 16.5% (at S6, aged 34-39). From univariable GEE analysis, women with depressive symptoms or a history of depression were more likely to report subsequent UI symptoms. This remained after adjusting for socio-demographic, body mass index, health behaviours and reproductive factors, with depressive symptoms associated with 37% higher odds (odds ratio 1.37, 95% CI 1.16 to 1.61) and history of depression with 42% higher odds (1.42, 1.17 to 1.74) of incidence of UI.

Conclusions: When woman seek treatment for UI symptoms, health professionals should consider her current or history of depression.

Keywords: urinary incontinence symptoms; depression; cohort study; young women; epidemiology

1. Introduction

Urinary incontinence (UI) has a detrimental impact on quality of life and overall health perception [1-9], and is estimated to affect between 25% and 45% of Australian women [8]. Studies have established that depression and UI are often comorbid [10-16], but the role of depression as a cause or consequence of UI is less clear. Furthermore, previous studies have primarily focussed on mid-age and older women, with the result that much less is known of the aetiology of UI and links between depression and the condition among younger women [5].

Findings from studies of UI with a wide age range of women has shown that various socio-demographic, and reproductive factors, and lifestyle factors, including being overweight or obese, having had a hysterectomy are associated with mixed (urge and stress) UI symptoms, while having given birth or being obese are linked with stress incontinence [4 8 9]. Depression, and superficially its temporal relationship with UI, was investigated by longitudinal study of mid-age women in the US that found the onset of UI was predicted by major depression at baseline, whereas UI did not increase the risk of subsequent depression [17]. This result is consistent with earlier research involving mid-age and older women, though the findings there suggested that the relationship of depression related to subsequent stress UI rather than urge UI [18 19].

This study draws on a decade of longitudinal data from a cohort of young Australian women to describe the prevalence of UI symptoms in this age group and to investigate the relationship between depression and subsequent reporting of UI symptoms, while controlling for a range of socio-demographic and reproductive factors, body mass index (BMI), and health behaviours.

2. Methods

2.1 Study population

The Australian Longitudinal Study on Women's Health (ALSWH) is a broad-ranging, national prospective study of factors affecting health and wellbeing of Australian women. In 1996, wide-ranging baseline survey data were collected for more than 40000 women in three age cohorts: the 1973-78 cohort (aged 18 to 23 years in 1996) that is the subject of this study; the 1946-51 cohort; and the 1921-26 cohort. Women in the 1996 sample were randomly selected from the national health insurance database (Medicare), which includes all Australian citizens and permanent residents. Women from rural and remote areas were deliberately oversampled. Informed consent was obtained from all participants, and approval was obtained from ethics committees at the University of Newcastle and the University of Queensland. Further details of the recruitment methods and response rates have been described elsewhere [20].

2.2 Participants

The sample for this study is drawn from women in the 1973-78 cohort who provided data from survey 2 (S2) in 2000 onwards (as detailed symptoms of depression were not collected at the 1996 baseline survey): S2 (n=9688), S3 in 2003 (n=9081), S4 in 2006 (n=9145), S5 in 2009 (n=8200), and S6 in 2012 (n=7968). Less than five per cent of the women were excluded from the analysis due to omitting information on symptoms of urinary incontinence or depression. The final sample sizes in the current analysis were n= 9316, 8897, 8920, 7931 and 7809 for S2 to S6 respectively, with a restricted sample of 6461 women who provided data at all five surveys. All variables listed below were ascertained at each survey unless indicated otherwise.

2.3 Study outcome

At each survey S2 to S6, women were asked whether they had experienced leaking urine in the past 12 months. Response options were: never, rarely, sometimes, or often. Women were considered to have had UI symptoms at a particular survey only if they reported experiencing leaking urine 'sometimes', or 'often'.

2.4 Exposure variables

Depressive symptoms. These were measured using the Center for Epidemiologic Studies Depression Scale (CESD-10), a standardised scale designed to screen for depression symptoms experienced in the past week [21]. Scores range from 0 to 30, with scores 10 or higher indicating significant levels of depressive symptoms [21]. Thus, in the present study scores were dichotomised such that women were either identified as having depressive symptoms (CESD-10 scores of 10 and above) or not (scores below 10).

History of depression. At S2 women were asked "have you ever been told by a doctor that you have depression: in the last four years, more than four years ago." Women who provided an affirmative answer to either question were classified as having a history of depression.

Antidepressant use. At S2, S3, and S4 women were asked if they had used prescription medication for depression in the past four weeks. At S5 women were asked to write down the names of all their medications that they have taken in the last four weeks and these were classified as antidepressant or not according to the Anatomical-Therapeutic-Chemical (ATC) drug classification system.

2.5 Covariates

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The following variables were included in the analysis as potentially confounding variables [1] and were collected at every survey unless indicated otherwise: area of residence (urban, rural, or remote); highest educational attainment (year 12 or less, apprenticeship/certificate/diploma, university degree, or higher university degree); oral contraceptive pill use (yes or no); maternal age at first birth in years (nulliparous, less than 20 years, 20 to 25, 25.1 to 30 years, more than 30.1 years); number of deliveries – reported at S6 – during which a vaginal tear requiring stitching occurred (0, 1, or 2 or more tears); and parity (0, 1, 2 or 3 or more children).

Body mass index (BMI) was calculated, from self-report weight and height, as weight (in kg) divided by height squared (in metres). BMIs were classified as: underweight (BMI <18.5), acceptable weight (BMI ≥18.5 and <25), overweight (BMI ≥25 and <30), obese (BMI ≥30) [9]. A physical activity score was derived from questions on frequency and total duration of various types of activity (inactive, low, moderate, high) [22]. Cigarette smoking was classified as none, past, or current smoker; and alcohol consumption as non-drinker, rarely, low-risk or risky, high-risk drinker [23].

2.6 Data analysis

The prevalence of UI symptoms at each survey over the study period (S2 to S6) was calculated using the restricted sample of women from the cohort who responded to all five surveys with respect to UI symptoms and depression.

The incidence of UI symptoms at a particular survey was defined by the presence of symptoms at that survey and absence of symptoms at all preceding surveys. Chi-squared analyses were used to compare the characteristics of women at S2 who developed UI symptoms between S3 and S6 with those who remained symptom-free.

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Generalised estimating equation (GEE) models were then used to relate each of depressive symptoms, use of antidepressant, history of depression (at S2), socio-demographic characteristics, reproductive factors, and BMI and health behaviours reported at S2 to S5 with the incidence of UI symptoms at the immediately subsequent survey (S3 to S6). The GEE model was used to handle the multiple observations from each woman. The analyses were performed using the GENMOD procedure in SAS with a logit link function and an exchangeable correlation structure. Women without UI symptoms were considered as the reference category.

To obtain a fully adjusted model relating depression with the incidence of UI symptoms the analysis was carried out in a series of steps. First the univariable GEE analysis was repeated but using the restricted sample of women with responses on UI symptoms across all the surveys to identify unadjusted associations between the incidence of urinary incontinence and each exposure: depressive symptoms, history of depression, use of antidepressant; and confounding variables: socio-demographic factors, reproductive factors, BMI and health behaviours. Factors that were significant at the 10% level with the incidence of urinary incontinence were then selected for inclusion in the multivariable model to reveal the extent to which the effects of depression, history depression, and antidepressant use were associated with age and survey years (Model 1), then attenuated by reproductive factors (Model 2) and then attenuated further by socio-demographic factor, BMI, alcohol intake and physical activity level (Model 3). Statistical analysis was conducted using SAS version 9.2, and differences with p-values <0.05 were considered to be statistically significant.

3. Results

From the restricted sample, the prevalence of UI symptoms (Figure 1) increased with age from 6% at S2 when the women were aged 22-27 years to 16% by S6 (aged 34-39 years). Women with depressive symptoms (CES-D ≥10), however, reported a consistently higher prevalence of UI symptoms, rising from 9% at S2 to more than 21% at S6.

Similar results were evident for the incidence of UI symptoms (Table 1), which were reported by one in four women (24.6%) between S3 and S6, with differences evident across a range of characteristics. A higher percentage of those with depressive symptoms (27% compared with 22%, p<0.0001) or a history of depression (28% compared with 23%, p=0.001) developed UI symptoms between S3 and S6. In terms of potential confounders, difference in the percentage incidence of UI symptoms was also evident for educational attainment, age at first birth, parity, number of vaginal tears, use of oral contraceptive pill, BMI category, and physical activity level. Some evidence was found for differences in the incidence in UI symptoms according to alcohol intake (p=0.05).

Differences in incidence of UI symptoms were also quantified via univariable analysis (Table 2). Those with depressive symptoms were more likely to report UI symptoms between S3 to S6 (Odds Ratio 1.30; 95% CI 1.16, 1.46), with a similar result for those with a history of depression (1.28; 1.11, 1.48). For confounding factors, women with children were more than twice as likely to report UI symptoms compared with nulliparous women; as was also evident for pregnant women (2.06; 1.87, 2.28). Women with vaginal tears had higher odds of reporting UI symptoms, with this odds rising with one tear (1.68; 1.49, 1.88) to two or more (1.79; 1.52, 2.11). Women in the overweight BMI category also had higher odds of reporting UI symptoms (1.25; 1.10, 1.42), with this odds increasing further for those in the obese category (1.32; 1.13, 1.53).

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Other factors were associated with lower odds of UI incidence among women. The level of educational attainment was associated with lower the likelihood of reporting UI symptoms, with those who had university degree qualifications at a lower odds (university degree 0.82; 0.72, 0.93; higher degree 0.78; 0.67, 0.91) compared with women who had Year 12 or lower qualifications. Women with high physical activity level had one-third lower odds (0.64; 0.53, 0.76) of reporting UI symptoms, compared with inactive women. A similar magnitude of difference was evident for those taking oral contraceptives (0.65; 0.58, 0.72). For alcohol consumption, only women who were low risk drinkers had lower odds of reporting UI symptoms (0.78 0.66, 0.93) compared with non-drinkers.

In the fully adjusted model (Table 3), which accounted for the effects of socio-demographic, reproductive, and health behaviour factors identified in the univariable analyses, women with depressive symptoms or with a history of depression at S2 were more likely to develop UI symptoms in the subsequent surveys (OR 1.37; 1.16, 1.46; OR 1.42; 1.17,1.74 respectively).

4. Discussion

4.1 Main findings

Initial findings from the ALSWH 1973-78 cohort, indicated that women with depressive symptoms had a consistently higher prevalence of UI symptoms over the study period (from ages 22 to 27 years at S2 through to 34 to 39 years as S6) than women who did not report depressive symptoms.

Further investigation into the temporal relationship of depression with the incidence of UI symptoms indicated that after adjusting for a range of confounding factors, women with depressive symptoms at one survey had 37% higher likelihood of reporting UI symptoms in the

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immediately following survey. Similar results were evident for women who reported a history of depression. These findings for young women are consistent with previous research that has implicated depression as a risk factor for subsequent urinary incontinence in mid-aged and older women [17-19].

4.2 Strengths and limitations

The present study is strengthened by its ecological validity, due to the large, nationally representative sample and the longitudinal nature of the data, which allowed the comparison of symptoms over time. In addition, the prospective nature of data collection increased the accuracy of the current study's data, as it reduced sources of error that may be present in research requiring long-term recall, for example, when mid-age and older women are asked to remember the circumstances surrounding the onset of urinary incontinence. In this study, surveys occurred at three-year intervals but asked the women about their experience of UI symptoms in the previous 12 months, leaving a two-year gap. So it is possible range that a higher level of UI incidence would have been recorded if the entire period between surveys had been covered at the expense of requiring a longer recall of symptoms, but if this had any impact it would have likely increased rather than weakened the associations identified. A further strength of the study is the use of validated CESD-10 scale which is designed to measure depressive symptoms in the population.

However, several methodological limitations of the study should be noted. Women who had given birth or been pregnant less than one year prior to the survey time were excluded from the analyses. Consequently, the study may have lacked sufficient power to detect some associations for instance between antidepressants use and UI symptoms. Additionally, as it was a population based-study across large geographical areas, it was not possible to use a clinical diagnosis of urinary incontinence; instead UI symptoms were based on the participants' reports on the

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frequency of leaking urine. While we have categorised women who reported leaking urine "sometimes' or "often" as indicative of the presence of UI symptoms, we obtained similar results when we only considered women who reported "often". Nonetheless our findings are consistent with previous studies on older women, a range of socio-demographic, reproductive factors, BMI, and health behaviours were also identified as associated with the incidence of UI symptoms [17-19].

4.3 Interpretation

The relationship between depression and urinary incontinence can be explained via several possible mechanisms. Firstly, both depression and urinary urge incontinence may arise from abnormalities in serotonin function. While a strong body of evidence supports a role of depleted serotonin levels in some types of depression [24-26], there is also a purported link between lower serotonin levels and enhanced bladder activity via the micturition reflex [27]. This link has been demonstrated in animal models [27 28]. Secondly, individuals with depression have been observed to have increased activation of the hypothalamic-pituitary pathway and the sympathetic nervous system [26]. Melville et al [17] speculate that over activation of these systems over a prolonged period, resulting in excess cortisol and catecholamines, might have a physiological impact on bladder function, which could potentially play a role in the experience of urinary incontinence. It may also be that depression and urinary incontinence are being caused by a common neurochemical pathogenesis, since antidepressant medications such as duloxetine is known to manage both symptoms [29 30]. Another explanation could be that women with depressive symptoms were more likely to report UI symptoms although we have minimised the effect by considering depressive symptoms at survey prior to the report of UI symptoms.

5. Conclusions

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Findings from this study suggest that depression is associated with the development of urinary incontinence symptom. It has a significant public health implication for the prevention and treatment of urinary incontinence. For instance when women in their twenty or thirties, seek advice or treatment on their UI symptoms, health professions should consider the possibility that depression and a history of depression may play a role in development of the condition.

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Contributors

All authors have contributed to the study and approved the final version of this manuscript.

GDM designed the study, conducted the analysis and drafted the manuscript. MB assisted with

manuscript preparation. GCHG and TH contributed to study design and assisted with manuscript

preparation.

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Figure captions

Figure 1 Percentage of women reporting of urinary incontinence symptoms in surveys 2 – 6 by Center for Epidemiologic Studies Depression Scale (CES-D) scores (n =6461)

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Table 1 Characteristics of women at Survey 2 (aged 22-27) and incidence of urinary incontinence between Surveys 3 and 6

Characteristic	N	UI symptom-free	Incidence of UI symptoms	p-value
Depression				<0.0001
CES-D 10 <10	4728	78.0	22.0	
CES-D 10 ≥10	1733	73.1	27.0	
History of depression				0.001
No	5749	77.4	22.6	
Yes	852	72.3	27.7	
Use of antidepressants				0.06
No	6306	77.0	23.0	
Yes	269	72.1	27.9	
Area of residence				0.104
Urban	3726	77.4	22.6	
Rural	2664	76.2	23.8	
Remote	246	72.0	28.1	
Educational attainment				0.015
Year 12 or less	1997	75.5	24.5	
Apprenticeship/Certificate/ Diploma	1535	75.2	24.8	
University Degree	2497	78.8	21.2	
Higher University Degree	439	78.6	21.4	
Age at first birth, years				<0.0001
Nulliparous	1843	90.7	9.3	
Less than 20.0	235	78.7	21.3	
20.0 to 25.0	792	77.0	23.0	
25.1 to 30.0	1989	73.9	26.1	
30.1 to 36.0	2306	78.9	21.1	
Parity				
Nulliparous	4702	80.9	19.1	<0.0001

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1	981	73.0	27.0	
2	630	70.8	29.2	
3 or more	229	71.2	28.8	
Number of vaginal tears				<0.0001
0	2607	82.1	17.9	
1	2066	72.6	27.4	
2 or more	685	69.2	30.8	
Oral contraceptive pill use				<0.0001
No	3065	76.4	23.6	
Yes	3218	80.6	19.4	
Body mass index				<0.0001
Underweight	398	82.4	17.6	
Acceptable weight	3963	78.1	21.9	
Overweight	1199	76.0	24.0	
Obese	588	71.1	28.9	
Physical activity levels				0.003
Inactive	581	70.9	29.1	
Low	2244	76.6	23.4	
Moderate	1586	77.7	22.3	
High	2114	78.1	22.0	
Smoking status				0.166
Never	4006	77.6	22.4	
Ex-smoker	922	75.2	24.8	
Current smoker	1690	75.9	24.1	
Alcohol intake				0.050
Non-drinker	4094	77.8	22.3	
Low risk drinker	509	72.9	27.1	
Rarely drinks	1785	75.7	24.3	
Risky drinkers	244	75.4	24.6	

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Table 2 Unadjusted odds ratios (95% confidence intervals) for the risk of developing urinary incontinence symptoms over successive surveys from 3 to 6 in young women (n=24,939 observations)

Characteristic		Odds ratio	p-value
Age (SD) (y)		1.10 (1.06, 1.13)	<0.001
Depression			<0.001
	CES-D 10 <10	Reference	
	CES-D 10 ≥10	1.30 (1.16, 1.46)	
History of depression			0.0007
	No	Reference	
	Yes	1.28 (1.11, 1.48)	
Use of antidepressant			0.3
	No	Reference	
	Yes	1.12 (0.90 – 1.40)	
Area of residence			0.006
	Urban	Reference	
	Rural	1.18 (1.07, 1.30)	
	Remote	1.09 (0.85, 1.39)	
Educational attainment			0.0002
	Year 12 or less	Reference	
	Apprenticeship/Certificate/Diploma	0.99 (0.87, 1.13)	
	University Degree	0.82 (0.72, 0.93)	
	Higher University Degree	0.78 (0.67, 0.91)	
Age at first birth, years			<0.001
	Nulliparous	Reference	
	Less than 20.0	2.91 (2.18, 3.88)	
	20.0 to 25.0	2.82 (2.31, 3.44)	
	25.1 to 30.0	3.09 (2.92, 3.64)	
	30.1 to 36.0	2.39 (2.03, 2.81)	
Parity			<0.0001
	Nulliparous	Reference	

	1	1.57 (1.19, 2.08)	
	2	2.16 (1.67, 2.80)	
	3 or more	2.30 (1.76, 3.01)	
Number of vaginal tear			<0.0001
	0	Reference	
	1	1.68 (1.49, 1.88)	
	2 or more	1.79 (1.52, 2.11)	
Oral contraceptive pill use			<0.0001
	No	Reference	
	Yes	0.65 (0.58, 0.72)	
Body mass index			0.0001
	Underweight	0.88 (0.65, 1.19)	
	Healthy Weight	Reference	
	Overweight	1.25 (1.10, 1.42)	
	Obese / Very Obese	1.32 (1.13, 1.53)	
Physical activity levels			<0.001
	Inactive	Reference	
	Low	0.82 (0.70, 0.97)	
	Moderate	0.75 (0.63, 0.90)	
	High	0.64 (0.53, 0.76)	
Smoking status			0.5
	Never	Reference	
	Ex-smoker	1.07 (0.94, 1.22)	
	Current smoker	0.97 (0.85, 1.12)	
Alcohol intake			0.003
	Non-drinker	Reference	
	Low risk drinker	0.78 (0.66, 0.93)	
	Rarely drinks	0.93 (0.77, 1.12)	
	Risky drinkers	1.02 (0.76, 1.37)	
Pregnancy status			<0.001
	Not Pregnant	Reference	
	Pregnant	2.06 (1.87, 2.28)	

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Table 3 Odds ratios (95% confidence intervals) for the associations between depression (depressive symptoms and history of depression†) at Surveys 2 to 5 and the risk of having urinary incontinence symptoms from Surveys 3 to 6 among young women (n=12450 observations)

Risk factors	Model 1		Model 2		Model 3	
	Odds ratio	p-value	Odds ratio	p-value	Odds ratio	p-value
Depressive symptoms at preceding survey		0.0001		0.0002		0.0004
CES-D 10 <10	Reference		Reference		Reference	
CES-D 10 ≥10	1.38 (1.19, 1.62)		1.38 (1.18, 1.62)		1.37 (1.16, 1.61)	
History of depression		0.0002		0.0005		0.001
No	Reference		Reference		Reference	
Yes	1.49 (1.24, 1.80)		1.45 (1.20, 1.76)		1.42 (1.17, 1.74)	

†history of depression was only asked at survey 2.
Model 1: adjusted for age and survey year
Model 2: includes depression, history of depression and adjusted for age, survey, reproductive factors (oral contraceptive pill use; currently pregnant, age at first birth and number of vaginal tears); Model 3: all variables in model 1 and education, area of residence, body mass index, alcohol intake, and physical activity level.

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Ethics

This project has been approved by the University of Newcastle's Human Research Ethics Committee, approval numbers: H-076-0795 and H-2012-0256, and the University of Queensland's Medical Research Ethics Committee, approval numbers: 2004000224 and 2012000950.

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Contributors

All authors have contributed to the study and approved the final version of this manuscript. GDM designed the study, conducted the analysis and drafted the manuscript. MB assisted with manuscript preparation. GCHG and TH contributed to study design and assisted with manuscript preparation.

Competing interests

All authors have no conflict of interests.

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