Association between parity and the risk for urinary incontinence in women
A meta-analysis of case–control and cohort studies

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Abstract

Urinary incontinence (UI) is a common complaint for adult female. Cross-sectional studies suggested parity may link with UI, but the association between them was not well-established. We conducted a meta-analysis to investigate the association between parity and UI.

Medline and Embase were searched for eligible case–control and cohort studies about parity and UI. Two authors screened the literature and extracted the data independently. Odds ratio (OR) was used as the measure of the effect of parity on UI. We pooled the ORs of different number of parity by a random-effect model. Subgroup analysis was conducted by a subtype of UI. Sensitivity analysis was conducted to see whether the results were stable.

Thirteen studies (8 cohorts and 5 case–controls) were included in our meta-analysis, with a total of 74,883 adult females. Our meta-analysis showed that compared with nulliparity, ORs of women with 1, 2, and ≥3 parity were 1.43 [95% confidence interval (95% CI): 0.90–2.28; $I^2=81.4\%$; n=4], 1.50 (95% CI: 1.02–2.20; $I^2=82.5\%$; n=4), and 1.58 (95% CI: 1.22–2.03; $I^2=70.1\%$; n=7) compared with nulliparity. The OR for any multiparity to nulliparity was 1.68 (95% CI: 1.39–2.03; $I^2=0\%$; n=4). Subgroup analysis showed that parity was associated with an increased risk of stress UI (OR=2.32, 95% CI: 1.41–3.81; $I^2=0\%$; n=2; 1 compared with null parity) but not urgent UI; However, the definition of parity varies across studies and studies defined parity as delivery times showed higher pooled OR than those not. Sensitivity analysis showed our results were stable.

Current evidence suggested that parity was associated with an increased risk of overall and stress UI but not urgency UI, though the definition of parity may differ. Higher parity may have a more significant effect on overall UI. Standardized definition of parity is needed.

Abbreviations: CI = confidence interval, OR = odds ratio, UI = urinary incontinence.

Keywords: meta-analysis, parity, urinary incontinence

1. Introduction

Urinary incontinence (UI) is a common complaint, particularly in postpartum and aging women.[1] The prevalence of UI in women varies across regions and populations, ranging from 10.8% to 79% among adults.[2] According to the International Continence Society, UI is defined as any involuntary leakage of urine.[3] There are 3 types of UI: stress UI, which is due to effort, physical exertion, or sneezing or coughing; urgency UI, which is associated with urgency; and mixed UI, which is a combination of both.[4]

Demographic characteristics (e.g., age), lifestyle habits (e.g., smoking), and baseline medical conditions (e.g., depression), obstetric characteristics (e.g., pregnancy) may be considered as important risk factors for UI.[5–8] Large cross-sectional surveys have suggested that multiparity was associated with a higher prevalence of UI.[5,9–12] Pregnancy and childbirth were also considered as risk factors for stress UI in some review articles.[4,13] However, due to the limitation of such type of studies (cross-sectional), current evidence can only support the potential association between parity and UI but not their causal relationship.[14] Moreover, the results of the cross-sectional study may be at risk for selective bias.[14] Whether parity causes UI or UI is an effect of parity is unclear.

On the basis of a literature search, we found no comprehensive evidence on the relationship between parity and UI. To establish the potential causation between parity and UI, a meta-analysis was conducted based on case–control and cohort studies of the adult population. Moreover, whether higher parity has significantly affected UI was validated.

2. Methods

This meta-analysis was conducted in accordance with the guidelines of the MOOSE Statement.[15] This study does not involve ethics, as it is based on the analysis of secondary evidence.

2.1. Eligibility criteria

In the present study, we included case–control and cohort studies that investigated the relationship between parity and the risk for UI. The population was limited to adult women. The exposure of interest was multiparity (compared with nulliparity or 1 parity), and the primary outcome was any type of UI. Cross-sectional studies were not included because they are descriptive and mainly used to describe prevalence. Moreover, they are not suitable for cause-and-effect analysis.[14] For cohort studies, only those that reported about the relationship between parity and risk of UI incidence were considered. Parity was defined as the number of offspring a female has borne, according to the MeSH term provided by PubMed. However, as the Child Health Epidemiology Reference Group (CHERG) Small-for-Gestational-Age-Preterm Birth Working Group of Johns Hopkins Bloomberg School of Public Health, parity was defined as number of live births.[6] Both of the terms were treated as parity in current meta-analysis.

2.2. Literature search and screening

We searched MEDLINE (1974 to February 12, 2018) and Embase (1946 to February 08, 2018) for potential publications without any language limitations. MeSH terms and free text words were combined to develop the search strategy. These mainly included "parity" [MeSH], "multiparty," "urinary incontinence" [MeSH], and "incontinence." The full search strategy is presented in the Supplementary file, http://links.lww.com/MD/C332.

Two authors (Z.H-H and G.Y-L) searched for eligible studies by reviewing the title and abstract and then the full text. For title and abstract reviewing, studies that were obviously not related were excluded. Conference abstracts, gray literature, and letters to the editor were not considered. Any disagreements were solved via discussion. If consensus is not reached, a third author was asked for judgment (L.T-Z).

2.3. Data extraction

Data were extracted by one author (Z.H-H) and then reviewed by another author (B.S). The following information about each study was collected: author's first name, year of publication, region, type of study, follow-up year for cohorts, control information for case–control studies, sample size, population characteristics (e.g., mean age), type of UI, number of parity, effect sizes, and variables that were controlled in the statistical analysis. For the effect sizes, we extracted the one controlled for most confounding variables. Any disagreements were reviewed by the 2 authors. The corresponding authors of previous studies that did not report any relevant information were contacted for potential data.

2.4. Quality assessment

We assessed the quality of the selected studies using the Newcastle–Ottawa Scale (NOS), which was widely used for quality assessment in the meta-analysis of observational studies.[16] This scale contains 9 items for both case–control and cohort studies. One star was assigned to each item if it met the standards. Otherwise, no star was assigned to the items. A study with more stars indicates higher scientific quality. A study with ≥7 stars was a high-quality study, whereas a study with ≤4 stars was a low-quality study. Quality assessment was performed concurrently by 2 authors (Z.H-H and Y.Z-H).

2.5. Statistical analysis

There were 2 types of studies and some of them used odds ratio (OR). Meanwhile, the others used risk ratio (RR) to measure the effect. Then, we combined them as OR by treating all RRs as OR. This was reasonable because the incidence rate of UI is less than 10%, and the RR was approximately equal to OR.[17]

Most studies presented the results in a categorical manner in which each number of parity corresponds to an OR compared with reference parity. We combined these ORs by category, as it is inappropriate to combine all the ORs with different categories. In detail, we combined the ORs of 1 parity, 2 parity, and ≥3 parity on UI separately from the selected studies. This allows us to detect the different impacts of parity number on the risk for UI. For studies reporting results by the subtype of UI instead of the overall UI, we combined the ORs of each subtype using the fixed-effect model as the overall OR for UI. The random- or fixed-effect model was used in the meta-analysis according to the amount of heterogeneity. I^2 that is higher than 30% indicated moderate to substantial heterogeneity. Thus, the random-effect model was used. Otherwise, the fixed-effect model was utilized.[18]

We also conducted a robust meta-regression analysis to assess the potential dose–response effect of parity on UI.[19] Sensitivity analysis was conducted by excluding low-quality studies and those that only included crude OR. Subgroup analysis was conducted according to the subtype of UI when the number of studies is sufficient. Considering the different definition of parity, subgroup analysis was also conducted according to the definition. Publication bias was identified using the funnel plot. All statistical analyses were performed using Stata version 12.0 (STATA, College Station, TX), and P value < .05 was considered statistically significant.

3. Results

We initially searched 2269 publications from the 2 databases, of which 341 were duplicates. Of the remaining publications, 1622 did not meet the criteria of the title and abstract. We further excluded 293 articles based on full-text reading. Finally, 13 eligible studies were included.[20–32] Figure 1 presents the screening details.

Among the 13 studies, 8 and 5 were cohort and case–control studies, respectively. For cohort studies, the follow-up period ranged from 3 to 18 years, and the median time was 9.5 (interquartile range: 4.75–11.25) years. For the 5 case–control studies, 4 used hospital-based control and 1 utilized community-based control. Seven studies were conducted in European countries, 3 in North America, 2 in South America, and 1 in Australia.

In total, 74,883 adult women were included in this meta-analysis. The mean age of the participants was 47.40 years, and the median age was 50 (interquartile range: 36.25–55.25) years. The total number of cases was not identified because some cohort studies did not report the information. The parity number ranged from 0 to ≥4. In terms of outcome, all types of UI, stress UI, and urgency UI were reported in 8, 5, and 2 studies, respectively. Table 1 depicts the basic characteristics of these studies.

The total quality of the selected studies ranged from 3 to 8. Of these studies, 6 were identified as high quality, 6 as moderate quality, and 1 as low quality (Table 2). The corresponding authors of the 2 potential studies were contacted.[33,34] However, they did not provide any relevant data.
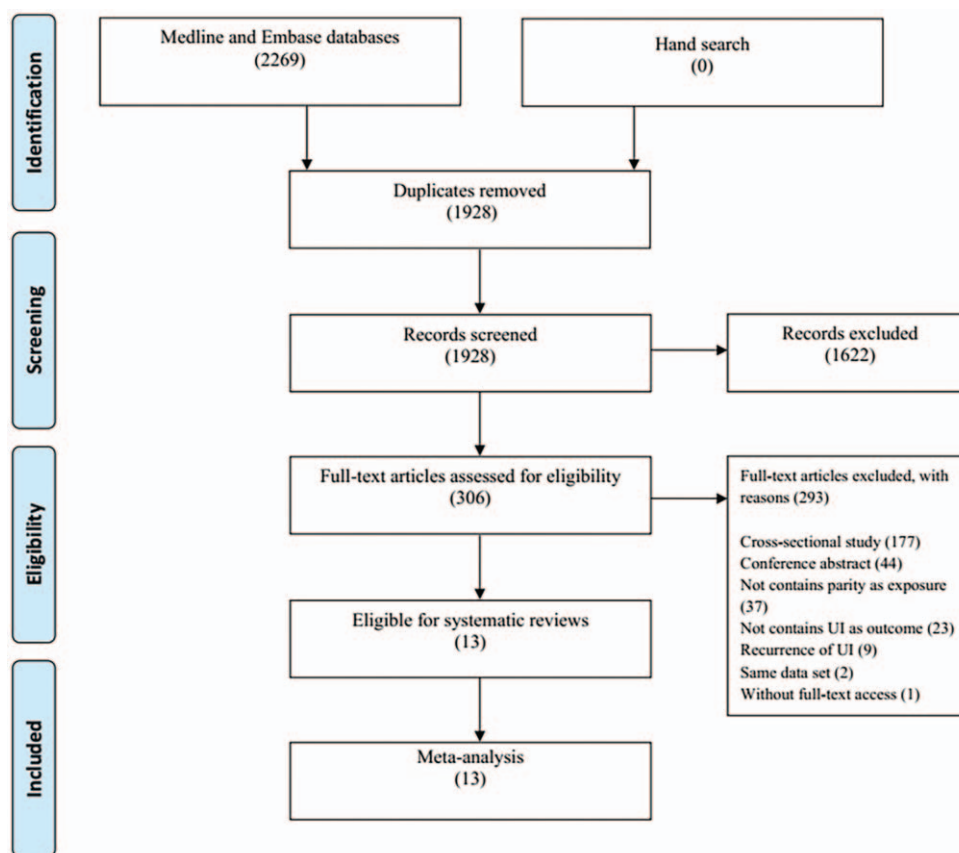
Figure 1. The flow chart.

3.1. Multiparity versus nulliparity for the overall UI

Of the 13 studies, 11 reported nulliparity as the reference parity. Moreover, 4 studies have shown the ORs of 1 parity compared to nulliparity, 4 on 2 parity, 6 on ≥3 parity, and 4 on any multiparity.

Our meta-analysis showed that the ORs of women with 1, 2, and ≥3 parity were 1.43 [95% confidence interval (95% CI): 0.90–2.28; $I^2 = 81.4\%$; n=4], 1.50 (95% CI: 1.02–2.20; $I^2 = 82.5\%$; n=4), and 1.58 (95% CI: 1.22–2.03; $I^2 = 70.1\%$; n=7) compared with nulliparity. The OR for any multiparity to nulliparity was 1.68 (95% CI: 1.39–2.03; $I^2 = 0\%$; n=4). Our results suggested that ≥2 parity may increase the risk of the overall UI for women compared with nulliparity. Figure 2 presents the forest plot of the results.

3.2. Meta-regression analysis

Thirteen studies can be used in the meta-regression analysis. These include another 2 studies with 1 parity as the reference. On the basis of the above-mentioned results, we centered all the reference parity to 0 to further explore the potential dose–response effect of parity on UI. Figure 3 presents the dose–response relationship. Our meta-regression analysis showed that, compared with nulliparity, each parity increase was associated with the increased risk of overall UI in women with ≥2 parity (OR=1.13, 95% CI: 1.05–1.22).

3.3. Sensitivity analysis, subgroup analysis, and publication bias

We excluded studies with low quality[21] and those that only provided crude OR.[24] Results showed significant decrease in heterogeneity, whereas the pooled ORs (random-effect) did not change (Figure S1, http://links.lww.com/MD/C332). Compared with nulliparity, the ORs of women with 1, 2, and ≥3 parity were 1.68 (95% CI: 0.99–2.85; $I^2 = 60.42\%$; n=2), 1.39 (95% CI: 1.08–1.78; $I^2 = 23.4\%$; n=2), and 1.55 (95% CI: 1.33–1.81; $I^2 = 0\%$; n=5), respectively.

A subgroup analysis was conducted considering the type of UI. There were 5 studies that focused on stress UI and 2 studies reported about urgency UI. We only combined the ORs of stress UI but not those of urgency UI because of the heterogeneous parity number. Our subgroup analysis showed that parity was significantly associated with the increased risk of stress UI, regardless of the parity numbers (OR=2.32; 95% CI: 1.41–3.81; $I^2 = 0\%$; n=2; 1 parity compared with null parity), as shown in Fig. 2. However, none of the 2 studies reported an association between urgency UI and parity (Fig. 4).

Of the 13 studies, 6 did not clarify the definition of parity, 5 defined parity as delivery times, 1 defined parity as number of babies, and 1 defined parity as number of term pregnancies. Subgroup analysis showed that, for studies defined parity as deliver times, the ORs were larger than those without definition or with other definitions, but there were no substantial changes of

Table 1

Basic characteristics of included studies.

Ref.	Region	Study type, follow-up	Sample	Population	Parity (Definition)	Risk of UI	Type of UI	Adjustments
Altman et al[20]	Sweden	Cohort study, 10 y	229	Primiparous women, Mean age (SD): 29.9 (4.1)	Null (No definition)	Reference	SUI	Age, maternal weight, fetal weight, history of perineal rupture, history of instrumental deliver
					1	2.4 (1.2, 4.3)		
					2	1.7 (0.8, 1.9)		
					3 to 4	1.9 (0.8, 3.1)		
Byles et al[21]	Australian	Cohort study, 9 y	9397	Old women, aged from 70 to 75 y	Null (No definition)	Reference	Any type	Survey time, area, diabetes, dementia, stroke, BMI, fall, visits to general practitioner, physical ability, urine burns or stings, constipation, prolapse, hysterectomy
					1	0.83 (0.65, 1.06)		
					2	0.98 (0.80, 1.19)		
					3 or more	1.09 (0.91, 1.31)		
Devore et al[22]	America	Cohort study, 4 y	9994	Female registered nurses, aged 25–55 y, with diabetes	Null (No definition)	Reference	Any type	Age, race, BMI, physical activity, postmenopausal hormone use, diuretic use
					3 or more	1.39 (1.04, 1.85)		
Ebbesen et al[23]	Norway	Cohort study, 11 y	42,598	Nord-Trøndelag resident, aged 20 y or above, mean age was 57.6 y	Null (No definition)	Reference	Any type	Age, BMI, weight change, smoking
					1	1.37 (1.04, 1.79)		
					2	1.28 (1.03, 1.61)		
					3 or more	1.56 (1.26, 1.95)		
Herrmann et al[24]	Brazil	Cohort study, 3 y	120	Pregnant women beyond 26 weeks, aged from 20 to 50 y	1 (Delivery times)	Reference	SUI	Crude
					2–3	1.37 (1.04, 1.79)		
					4 or more	1.28 (1.03, 1.61)		
Legendre et al[25]	French	Cohort study, 18 y	4127	Middle-aged (47–52 y) women worked for the French national power company	Null (No. of babies)	Reference	Any type	Weight, education, marital status, alcohol intake, depression, physical mobility, sleep, menopause, hysterectomy
					1 or more	1.64 (1.19, 2.27)		
Leroy et al[26]	Brazil	Case–control study, hospital-based control	77 cases, 267 controls	Puerperal women up to 90 d, mean age (SD): 25.9 (7.7)	Null (Delivery times)	Reference	Any type	Age, UI during pregnancy, types of previous birth, newborn's head circumference, weight, gestational age at birth, smoking, and constipation
					1 or more	2.26 (1.22, 4.19)		
	America	Case–control study, hospital-based control	1204 cases, 931 controls	Primary care patients 40 y of age and older	Null (No definition)	Reference	Any type	
					1 or more	1.87 (1.34, 2.60)		
Hirsch et al[27]	Denmark		275 cases, 381 controls		1 or more	1.20 (0.71, 2.01)	UUI	Age, BMI, diabetes, and birth history
					Null (Delivery times)	Reference		

Table 1
(continued).

Ref.	Region	Study type, follow-up	Sample	Population	Parity (Definition)	Risk of UI	Type of UI	Adjustments
Moeller et al[28]		Case–control study, community-based control		Women aged 40–60 y from and urban and rural county	1 2	2.2 (1.0, 4.9) 3.9 (1.9, 8.0)	SUI	Age, BMI, physical activity, abortion, prolapse, hysterectomy cystocele repair, straining at stool, diuretics, antibiotics
	Italy	Case–control study, hospital-based control	1062 cases, 1143 controls	Women in first level gynecological centers aged 40–88 y for cases, and 40–86 y for controls. Results based on vaginal birth	3 4 or more Null (Delivery times) 1–2 3 or more Null	4.5 (2.1, 9.5) 7.8 (3.3, 18.4) Reference 0.8 (0.4, 1.6) 0.8 (0.4, 1.7) Reference	UUI	
Parazzini et al[29]					1–2 3 or more Null	5.4 (1.9, 15.0) 5.1 (1.8, 14.6) Reference	SUI	Age, delivery type, education, BMI, obstetric history and hormonal replacement therapy
					1–2 3 or more	1.6 (1.0, 2.6) 2.2 (1.3, 3.7)	Mixed UI	
Pizzoferrato et al[30]	French	Cohort study, 12 y	236	Nulliparous women at a term of 37–41 wks, mean age was 41.3 y	1 (Delivery times)	Reference	Any type	Age, BMI, first children's weight, model of 1st delivery
Skoner et al[31]	Portland	Case–control study, hospital-based control	94 cases, 46 controls	Patients in 3 private gynecological practices	2 or more Null (Number of term pregnancies)	1.63 (0.62, 4.25) Reference	SUI	Delivery model, labor, anesthesia, birth weight, family history, genitourinary and related factors, smoking, alcohol, caffe, water intake, weight gain, constipation, cough
Waetjen et al[32]	America	Cohort study, 5 y	2702	Community-based women at 7 clinical sites, aged 40–55 y	4 or more Null (No definition) 1 or more	1.18 (0.46, 3.11) Reference 1.31 (0.88, 1.96)	Any type	Age, race, social support, BMI, waist circumference, medical conditions, health status

BMI = body mass index, UI = urinary incontinence.

Table 2

Risk of bias of included studies.

Ref.	Study type	Selection				Comparability		Exposure/Outcome			Total score
Altman et al[20]	Cohort study	★	★	★	★	★	★	–	★	–	7
Byles et al[21]	Cohort study	–	★	–	–	–	★	–	★	–	3
Devore et al[22]	Cohort study	–	★	–	★	★	★	–	★	–	5
Ebbesen et al[23]	Cohort study	★	★	★	★	★	–	–	★	–	6
Herrmann et al[24]	Cohort study	★	★	★	★	–	–	★	★	–	6
Hirsch et al[25]	Case–control	★	★	★	★	★	–	–	★	★	7
Legendre et al[26]	Cohort study	★	★	★	★	–	★	–	★	★	7
Leroy et al 2016[27]	Case–control	★	–	–	★	★	★	–	★	–	5
Moeller et al[28]	Case–control	★	★	★	★	★	★	–	★	★	8
Parazzini et al[29]	Case–control	★	★	–	★	★	★	–	★	★	7
Pizzoferrato et al[30]	Cohort study	★	★	–	★	★	–	–	★	–	5
Skoner et al[31]	Case–control	★	★	–	–	–	★	★	★	–	5
Waetjen et al[32]	Cohort study	★	★	★	★	★	★	–	★	★	8

The most important factors that should be controlled were age and BMI; the sufficient follow-up rate (cohort)/response rate (case–control) was defined as 80% or more.
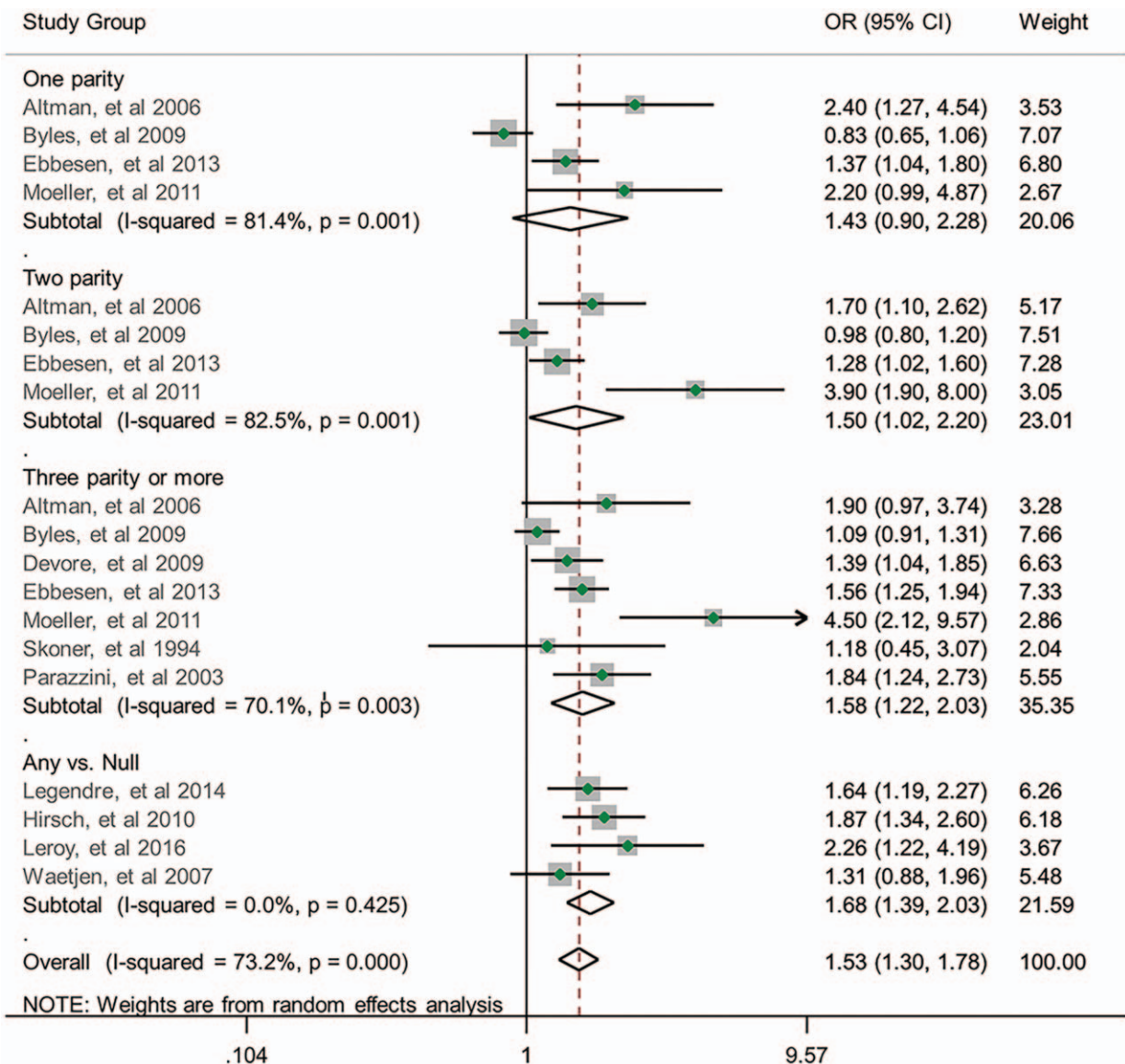

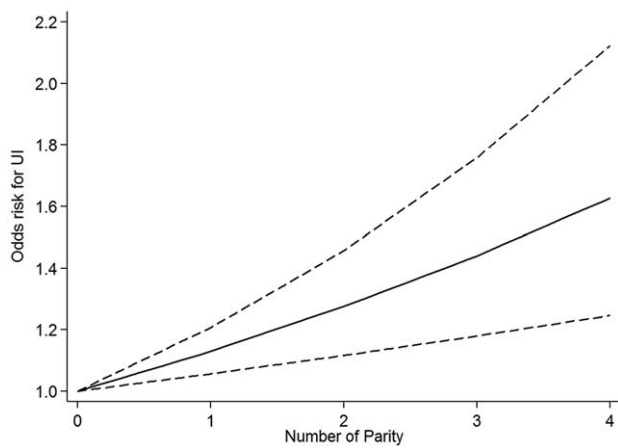Figure 2. Relationship between parity number and risk of UI.

Figure 3. Dose–response relationship between parity and UI.

the significance. The amount of heterogeneity was decreased (Figure S2, http://links.lww.com/MD/C332).

We used the data of women with ≥3 parity for publication bias. Funnel plot suggested possible publication bias (Figure S3, http://links.lww.com/MD/C332).

4. Discussion

To the best of our knowledge, this is the first meta-analysis that investigated the relationship between parity and the risk of UI. In this meta-analysis, we combined the effect sizes of the cohort and case–control studies for the assessment of a potential causation relationship between parity and UI. For overall UI, women with ≥2 parity had an increased risk for UI, and every increase in parity would increase the ORs for UI to approximately 12%. Meanwhile, for stress UI, women with ≥1 parity also had an increased risk for UI. However, we did not find any association between parity and urgency UI.

In our meta-analysis, 1 parity was associated with the increased risk of stress UI but not overall UI compared with nulliparity. This result may be partly attributed to the overall UI that includes both stress and urgency UI, and the later offsets the impact of parity on stress UI. Another possibility is the limited number of studies and sample size for overall UI with insufficient power to detect the difference.

UI is a disease associated with multiple mechanisms. Bladder overactivity, poor bladder control, and pelvic floor musculature impairment were all the direct causes of UI.[35] The results are attributed to pelvic floor musculature and connective tissue injury during the process of parturition that influences the normal urinary continence function.[4] However, this was also highly dependent on the type of delivery. In some studies, caesarean delivery was not associated with risk of UI.[29,36] In our
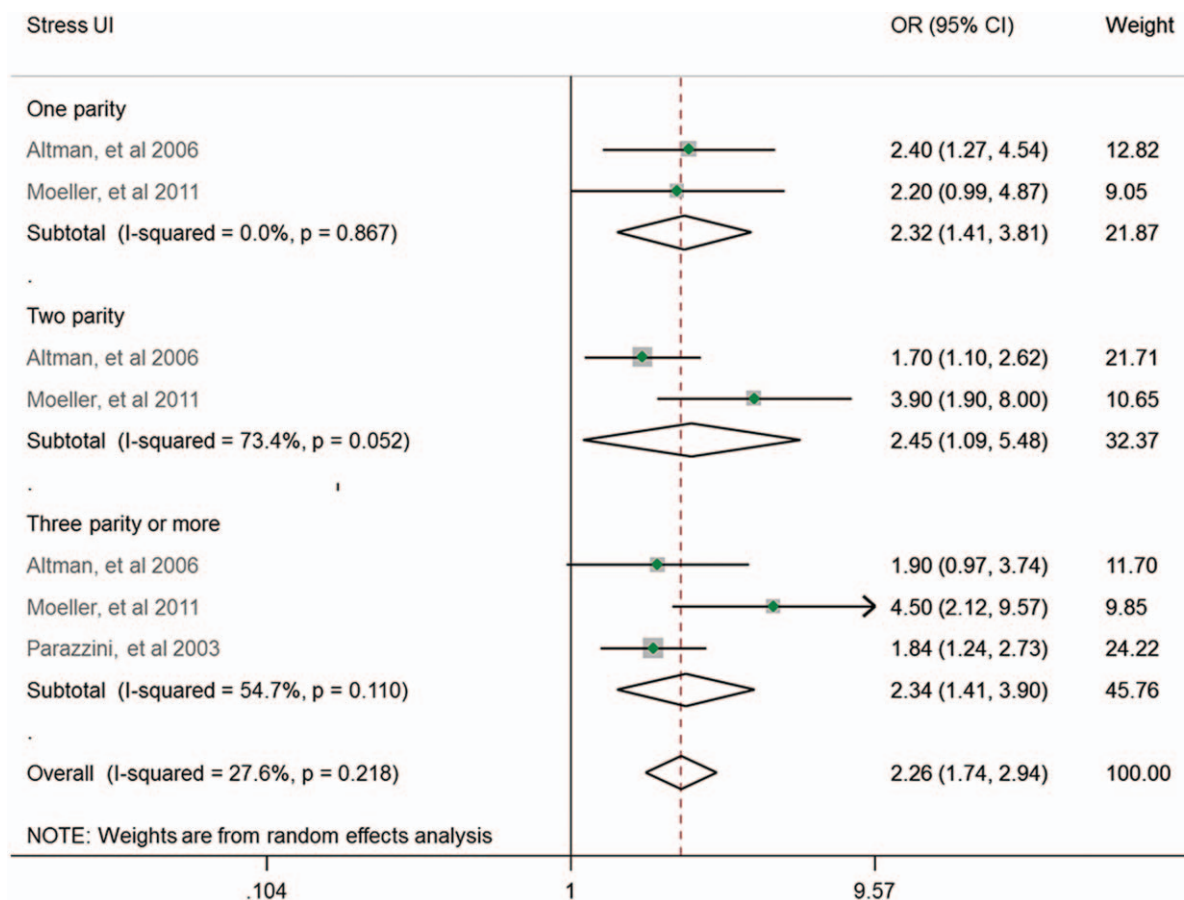

Figure 4. Subgroup analysis by type of UI.

meta-analysis, most of the studies did not report about the delivery type. As a result, the identification of the effects of delivery type becomes challenging.

In our meta-analysis on the overall UI, substantial heterogeneity was observed among the studies. Then, further sensitivity and subgroup analyses were conducted, and results showed a significant decrease in heterogeneity. Thus, it is reasonable to conclude that study quality, adjustment of confounding variables, the types of UI, and definition of parity are the main causes of heterogeneity. It is notable that, in subgroup analysis by definition of parity, we found studies defined parity as delivery times have larger ORs than those without definition or with other definitions. This indicates the definition of parity may influence the summarized results that delivery times have higher extent of harm for UI. Further original studies should pay attention with the definition.

Our meta-analysis has several key strengths. First, unlike previous cross-sectional study, case–control and cohort studies were included, and this allows us to detect the potential causation relationship between parity and UI. Second, we did not combine the ORs from different categories. Instead, we only combined the ORs with the same number of parity across studies. This ensures a statistically correct estimation of the confidence interval. More importantly, this method allows us to detect the impact of the different number of parity on UI. Third, we used a meta-regression analysis for dose–response effect estimation. Fourth, further analysis (sensitivity analysis) was conducted to ensure that the results were valid and clinically significant.

However, this study also has some limitations. In this meta-analysis, there were limited studies that reported about the relationship between parity and subtypes of UI, which makes it difficult to distinguish the difference in the effect of the 3 major types of UI. Furthermore, the categories differ across studies, and as a result, some information cannot be used in the current meta-analysis. For example, the study by Parazzini et al[29] considered 1 to 2 parity as one category, and such information cannot be combined in the 1 parity group or the 2 parity group. Moreover, publication bias was identified. Indeed, there were 2 other[33,34] potential studies. However, the corresponding authors of previous studies did not provide relevant data.

In conclusion, current evidence from case–control and cohort studies suggests that parity was associated with the increased risk of overall and stress UI but not urgency UI. Higher parity has a more significant effect on overall UI in a dose–response matter. However, these results should be interpreted with caution. Further high-quality cohort studies must be conducted to verify our results.

Author contributions

Z.H.H.: project development, search and screen literature, collect data, drafted the manuscript, revise manuscript; B.S: check the data, revise manuscript; G.Y-L: project development, screen literature, statistical analysis, and revise manuscript; Y.Z.H: quality assessment, revise manuscript; L.T.Z. and W.X.H. revise manuscript, provide professional guidance of UI.

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