

Worldwide Prevalence of Pelvic Organ Prolapse: A Systematic Review and Meta-Analysis

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Abstract

Background: The prevalence of pelvic organ prolapse is varied in different countries. For validating the results of numerous studies on the prevalence of Pelvic organ prolapse in the world, a meta-analysis study seems necessary to provide an accurate and valid prevalence for planners and researchers in this field. Therefore, we aimed to investigate the worldwide prevalence of pelvic organ prolapse using the meta-analysis method.

Methods: By using valid keywords, searching was done in ISI Web of Science, PubMed, Scopus, and Medline databases, and 22 articles were selected based on inclusion criteria between 2009 and 2021. The quality of articles was checked using The Joanna Briggs Institute (JBI) checklist. Meta-analysis was performed on collected data using Comprehensive Meta-Analysis Software (CMA, Version 2). Meta-analysis of data was done with a random-effects model. The heterogeneity of the study was checked using the I² index. Publication bias was assessed by the Egger test and funnel graph.

Results: The overall prevalence of included studies was 30.9% (95% confidence interval: 24.4-38.2%), (P<0.001, heterogeneity I2=99.8%). Meta-analysis of subgroups in studies that used a questionnaire to estimate the prevalence rate showed the prevalence was 25.0% and, in the studies, used the physical examination was 41.8%.

Conclusion: Studies carried out in different parts of the world have examined the prevalence of pelvic organ prolapse using different tools. Since some cases are asymptomatic, especially in the low stage of prolapse, physical examination of pelvic organ prolapse should be considered an essential tool in evaluating pelvic organ prolapse.

Keywords: Pelvic organ prolapse; Prevalence; Meta-analysis; Systematic review

Introduction

Pelvic organ prolapse (POP) occurs when one or more pelvic organs (the bladder, uterus, rectum, and small intestine) descend into the vaginal canal as a consequence of weakness in the pelvic support or dysfunction of the nerves, muscles, or both (1). POP is often associated with symptoms



of urinary tract dysfunction, such as urinary incontinence, Frequency, urgency, poor urine flow, delayed or forceful urination, incomplete bladder emptying, and recurrent urinary tract infection. In addition, it is related to vaginal pain, vaginal discharge, heaviness, bleeding, burning sensation, itching, dyspareunia, coital incontinence, and constipation (2-4).

Women who suffered from POP have a lot of problems in their sexual life including experiencing sexual discomfort, damaged genital body image, psychological problems and they are subject to domestic violence (5, 6). POP is one of the main causes of disability among women in high and low-income countries that can affect their quality of life (7, 8).

The prevalence varies in different countries. Heterogeneity in the prevalence of POP depends on environmental, behavioral, and ethnic factors (9, 10). This problem was common in high-income countries; however, it is expected that the problem will be even worse in low-income countries, because women in low-income countries are more likely to suffer from childbirth at a young age, multiple vaginal births, hard work and heavy lifting (7). Complaints of POP symptoms have increased in all countries over the past few decades (11), but in general, epidemiological studies of POPs are scarce because there is no standard and accurate method for assessing the presence or absence of POP and the severity of the symptoms.

Although epidemiological studies should be carried out according to standard criteria, most epidemiologic studies have been performed on POP based on a physical examination, self-report questionnaire, clinical population, or pre-surgery list, and this can estimate the rate of POPs less than actual, and the asymptomatic women will not be identified. Also, diagnosing and grading POP based on physical exams have been done in a variety of ways, including the Women's Health Initiative (WHI), Baden–Walker System, and Pelvic Organ Prolapse quantification system (POP-Q) (12). In the questionnaire-based survey, the prevalence of symptomatic POP was reported

2.9-25%, but increased to 76-75% in exam-based studies (13-17). Knowing the latest statistics on the prevalence of POP can help health planners to design appropriate programs to reduce the rate. However, in the searches, a new review study was not found. Hallok and Handa only reported a descriptive overview of prolapse and risk factors (18). Barber and Maher reviewed studies until 2009 (16). Also, Walker and Gunasekera's study examined only studies conducted until 2007, and no meta-analysis has been performed on the data (19).

Meta-analytical studies are important because of the increased sample size resulting from the combination of various studies, thus reducing the confidence intervals of these sizes and reducing the controversial results of past studies. Therefore, we aimed to review the prevalence of pelvic organ prolapse in the world.

Methods

This systematic review and meta-analysis followed the suggestions proposed by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement (20).

Search strategy

An electronic search was carried out using MeSH-based keywords including Epidemiology, Prevalence, Pelvic floor dysfunction, Pelvic organ prolapse, Pelvic floor disorder, Urine incontinence, fecal incontinence, and women in Web of Science, PubMed, Scopus, Medline, Cochrane electronic databases. There was no limitation on the location of the study. In the end, a manual search was done in references of the selected articles in Google Scholar to find relevant articles not found in the electronic search. The process of selecting the articles was done based on the (PRISMA) flowchart. Based on the search strategy and keywords, a list of all the articles in the mentioned databases was prepared. The researchers examined the titles of the articles obtained, and repetitive articles were deleted. Then, the title and abstracts of the remain-

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ing articles were carefully reviewed and irrelevant articles were rejected. Finally, the full text of the related articles was examined, and articles with inclusion criteria were selected. The papers were selected regardless of where the studies were conducted in the period of 2009-2021. In order to eliminate bias, two researchers independently (By ZHT and TM) carried out the searching process and extracting data. The process of reviewing and selecting the articles is shown in Fig.1.

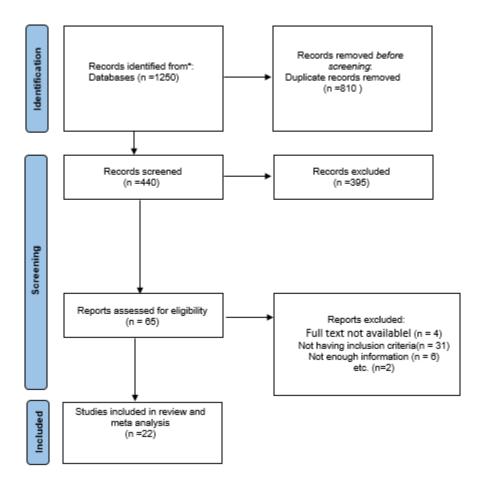


Fig. 1: PRISMA flow diagram of selection of studies process

Eligibility criteria

The inclusion criteria included descriptive population-based studies, which examined the prevalence of POP in the general population over the period 2009-2021. The exclusion criteria were studies that evaluated the prevalence of POP in a specific population, such as obese, postpartum, post-hysterectomy, post-menopause, athletes, articles published in other languages, academic articles, letters to the editor, articles presented at the conferences and articles not available in full.

Data extraction

For data extraction, a form was designed based on the purpose of the research. This form includes the first author, the year of publication, sample size, age range, method of data collection, and outcomes. After completing this form, the results of the analysis of articles were summarized and eventually reported (By ZHT and TKH).

Methodological quality assessment:

The quality of articles entered into this systematic review was checked using the Joanna Briggs Institute (JBI) checklist. This tool is a standard form for evaluating prevalence articles. This tool contains nine questions that are answered in a yes, no, and uncertain. The minimum and maximum scores for each study are zero and nine. Accordingly, studies are classified into three groups: low quality (0-3), moderate quality (4-6), and good quality (7-9) (21). In the case of disagreement between the two researchers on the quality of each article (ZHT and TM), it was resolved with the aid of a third researcher (By MS).

Data analysis

Meta-analysis was performed on collected data using Comprehensive Meta-Analysis Software (CMA) (version 2). The variance of each study was calculated based on the number of samples and the number of events using a binomial distribution with a 95% confidence interval. The heterogeneity among the studies was assessed using the inconsistency test (I2) in which values of less than 25%, between 25% and 75%, and more than 75% were considered as low, moderate and high

heterogeneity, respectively. The significance level was considered as P < 0.05. Due to the outstanding heterogeneity among the studies (99.8%), we used a random effect model to pool the prevalence rates. The sources of heterogeneity can be either clinical or methodological or a combination of the two. To explain the sources of heterogeneity, Subgroup analyses, and meta-regression were performed for age, the year of the study, and type of assessment tool. We applied Egger's test to assess for probable publication bias of POP prevalence.

Results

Among the 1250 articles found in the database research, 22 articles met the eligibility criteria. Four studies had moderate quality and the rest had good quality, and no articles were rated as low level with JBI criteria. Detailed information on the quality of articles is shown in Table 1.

Table 1: Assessment of the quality of 18 included studies with JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

Authors/ Ref- erence	Q1	Q2	Q3	Q4	Q5	Q6	<i>Q</i> 7	Q8	Q9	Total score
Pang/ (22)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Beketie/ (23)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Jokhio/ (24)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Gaddam/ (25)	U	Y	U	N	Y	Y	Y	Y	U	5
Li/ (26)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Belayneh (27)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Chen/(28)	Y	U	U	Y	Y	Y	Y	Y	Y	7
Masenga/ (7)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Dheresa/ (29)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Ghandour/ (9)	Y	Y	U	Y	Y	Y	Y	Y	Y	8
Akter/ (30)	Y	Y	U	Y	U	U	Y	Y	Y	6
Islam/ (31)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Zeleke/ (32)	Y	Y	Y	U	Y	U	Y	Y	Y	7
Elbiss/ (33)	Y	Y	Y	Y	Y	U	U	Y	Y	7
Direkvand/	Y	Y	U	Y	U	Y	Y	Y	U	6

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Table 1: Continued...

(35) Aytan/ (36)	U	Y	U	U	Y	Y	Y	Y	Y	7
Cooper/(37) Megabiaw/ (34)	U Y	N Y	U Y	U Y	Y Y	Y Y	Y Y	\mathbf{Y} \mathbf{Y}	N Y	4 9
Awwad/ (38)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Lien/(39)	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Miedel/ (40) Sliek- ertenhove/ (14)	Y Y	Y Y	9 9							

Y: Yes, N: No, U:Unclear

All studies had a cross-sectional design. The total number of participants in the 22 studies was 118,092. The prevalence varied in the different countries by type of assessing tool. The characteristics of studies that met meta-analysis criteria were presented in Table 2.

The global Pelvic Floor Bother Questionnaire (PFBQ), Questionnaire for Urinary Incontinence Diagnosis (QUID), POP and FI were assessed by the Pelvic Organ Prolapse Distress Inventory-6 (POPDI-6), and the Colorectal-Anal Distress Inventory-8 (CRADI-8), World Health Organization (WHO) assess symptomatic POP, Urogenital Distress Inventory (UDI), the Defecation Distress Inventory (DDI), Pelvic Floor Distress Inventory (PFDI-20), Pelvic Organ Prolapse Symptom Score (POP-SS).

The overall pooled prevalence based on the random effects model was 30.9% (95% confidence interval: 24.4-38.2%), (heterogeneity: I2=99.8%, P<0.001). Meta-analysis of subgroups using the random effects model method showed the prevalence of 25.0% in questionnaire-based studies, and 41.8% in physical exam-based studies (Figs. 2 and 3). The overall prevalence of POP based on the random effects model over the years (2009-2014) was 42.6% with a confidence interval of 27.9- 58.7%, and in the years (2015-2021) was 24.6% with a confidence interval of 18.3-32.2%, Which indicates the decrease in the prevalence of POP over time. In addition, the results of metaregression showed that with increasing age, the prevalence of POP is increased (Fig. 4).

Q1-Was the sample frame appropriate to address the target population?

Q2-Were study participants sampled in an appropriate way?

Q3-Was the sample size adequate?

Q4-Were the study subjects and the setting described in detail?

Q5-Was the data analysis conducted with sufficient coverage of the identified sample?

Q6-Were valid methods used for the identification of the condition?

Q7-Was the condition measured in a standard, reliable way for all participants?

Q8-Was there appropriate statistical analysis?

Q9-Was the response rate adequate, and if not, was the low response rate managed appropriately?

Table 2: Characteristics of the included studies

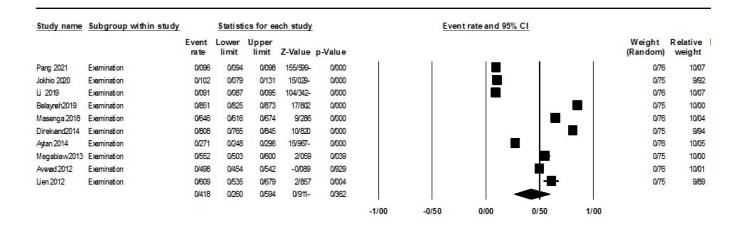
Authors/ Reference	Year	Country	sample size/ range of age/ mean age	Assessment Tool	Prevalence (%)	Other result/ risk factors
Pang/ (22)	2021	China	55477 aged ≥20 years/ 45.1	Examining and grading with POPQ and (PFDI-20) Questionnaire	By Question- naire: 21.9 By Examining: 9.6	Stage II: 7.5% Stage III: 1.7% Stage IV:0.4% Factors that had a meaningful relationship with POP: age and multiple vaginal deliveries
Beketie/ (23)	2021	Ethiopia	542/ Aged over 18 years/ 36	Researcher- made Ques- tionnaire	25.5	Factors that had a meaningful relation- ship with POP: Menopause, weight lifting greater than 10 Kg, parity, and number of vaginal deliver- ies
Jokhio/ (24)	2020	Pakistan	521/ aged 15 years or older/ 46	Examining and grading with Baden-Walker classification	10.3	Prolapse Stage I: 36.1% Stage II: 26.1% Stage III: 17.1% Stage IV:20.7% the most common POP being the cystocele grade I: 24.8% Anterior only genital prolapse occurred in 24.8%, anterior and posterior in 25.1%, posterior only 9.2% Factors that had a meaningful relationship with POP: Age and Parity
Gaddam/ (25)	2020	India	300/ 18-70/ 37.49±10.32	Researcher- made Ques- tionnaire	17.33	Factors that had a meaningful relation- ship with POP: Age, education, occupa- tion, number of children, mode of deliv- ery, BMI
Li/ (26)	2019	China	24848/ (20-99)/ 45.4±15.7	(PFDI-20) Questionnaire and Examining	By Question- naire: 9.23 By Examining: 9.10	Prolapse stage II: 7.55% Stage III: 1.52% Stage IV:0.16% Factors that had a meaningful relationship with POP: Age, Body Mass Index, Parity, Constipation, Smoking, Chronic Cough Diseases and Gynecological dis-
Belayneh (27)	2019	Ethiopia	824/ aged over18 years/ 44	Examining and grading with POPQ And (POP-SS) Questionnaire	By Question- naire: 46.7 By Examining: 85.1	ease Prolapse Stage I: 28.8% Stage II: 38.7% Stage III: 13.2% Stage IV:4.4% The prevalence of POP increased with increasing age and number of deliveries
Chen/(28)	2019	Nepal	14,469/ Age < 18 years old/ 33.5±8.2	Researcher- made Ques- tionnaire	8.0	The prevalence of POP increased with increasing age and number of deliveries
Masenga/ (7)	2018	Tanzania	1047/ (-)/ 46	Examining and grading with POPQ	By Examining: 64.6	Prolapse Stage I: 28.8% Stage II: 63.3% Stage III: 0.6% Stage IV:0.4% The anterior segment was the most prevalent.

Table 2: Continued...

						Factors that had a significant relationship with degree of POP: Age, number of pregnancies, number of delivery at home, education, being a
						farmer, heavy lifting more than 2 hours a day
Dheresa/ (29)	2018	Ethiopia	3432/ (-)/ 36.5±13	Researcher- made Ques- tionnaire	20.5	49.6% of the subjects had two or more types of POP.
Ghandour/ (9)	2016	Lebanon	900/ (-)/	Questionnaire (PFBQ)	44	Factors that had a significant relationship with POP:
· ·			49.6± 6.3			Age, number of pregnancies, education, smoking, diabetes, hypertension, heavy lifting during the day or work, body mass, history of hysterectomy Factors did not have a significant relationship with POP: Chronic cough, cesarean section
Akter/ (30)	2016	Bangladesh	787/ (more than 15)/ 40.1± 9/0	WHO ques- tionnaire	15.6	Factors that had a significant relationship with POP: Age, educational level, chronic lung dis-
Islam/ (31)	2016	Bangladesh	1590/ (30-59)/ 44.4± 8.5	QUID, (POPDI-6), CRADI-8 ques- tionnaire	16.2	ease, constipation The prevalence of urinary incontinence was: 23.7%, fecal incontinence: 5.3% Factors that had a significant relationship with POP:
						Age, Having three or more children, dia- betes
Zeleke/ (32)	2016	Australia	1517/ (65-75)/	(POPDI-6) Questionnaire	6.8	Factors that had a significant relationship with POP:
Elbiss/ (33)	2015	Saudi Ara- bia	71.5± 4.1 482/ (age more than 30 year)/ 38.2± 0.9	Researcher- made Ques- tionnaire	29.6	Obesity and parity Factors that had a significant relationship with POP: Age, education level, chronic lung disease, constipation, weight, occupation, weight
Megabiaw/ (34)	2013	Ethiopia	395/ aged at least 15 years/ 35	Examining and grading with POPQ And Researcher-made Questionnaire	By Question- naire: 6.3 By Examining: 55.1	of the baby Carrying heavy objects and having a history of prolonged labour were significantly associated with anatomical prolapse
Direkvand/ (35)	2014	Iran	365/ (-)/ 38.02± 8.99	Examining and grading with POPQ	80.8	Prolapse stage 0: 19.2% stage I: 20.0% Stage III: 60.8% The anterior segment was the most prevalent: 72.3% Factors that had a significant relationship with POP: Age, number of pregnancies, infant weight, body mass index, type of delivery, type of occupation Factors did not have a significant relationship with POP: constipation

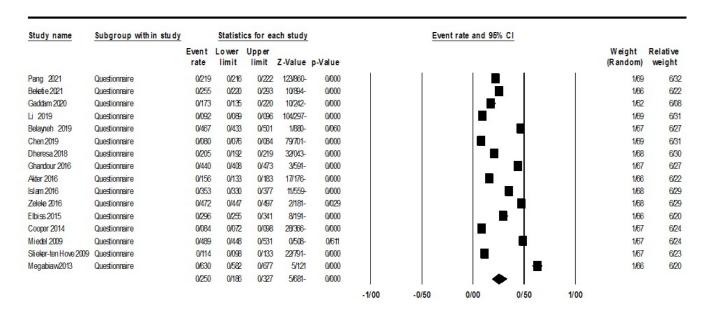
Table 2: Continued...

Aytan/ (36)	2014	Turkey	1320/	Examining and	27.1	Factors that had a significant relationship
			(-)/ 39/0± 11.1	grading with POPQ		with POP: Age, body mass index, parity, baby weight and waist to hip ratio
Cooper/(37)	2014	UK	1832/ over the age of 18 56.5 ± 17.7	Incontinence Questionnaire for vaginal symptoms ICIQ-VS	8.4	Previous pelvic floor surgery and age were statistically increased Vaginal symp- toms
Awwad/ (38)	2012	Lebanon	557/ 15- to 60 year- old/ 40.42±9.34	Examining and grading with POPQ And Researcher-made Questionnaire	49.8	39.3% had anterior vaginal wall prolapse, 16.1% had posterior vaginal wall prolapse, and 14.9% had apical/cervical prolapse. 30.6% of the women had a single organ affected. 18.1% had two organs affected, and 1.2% had three organs affected. (33.7%) had stage II prolapse, (14.5%) had stage III prolapse, and (1.6%) had stage IV prolapse. A history of fetal macrosomia, age, miscarriages, Menopause status, previous gynecological surgical operation, and BMI associated with a significant increase in the odds of POP
Lien/(39)	2012	Nepal	174/ (-)/ 40.4±14.9	Examining and grading with POPQ	60.9	93 (53.4%) of the women had stage II or greater cystocele, 63 (36.2%) had stage II or greater rectocele, and 37 (21.3%) had stage II or greater uterine prolapse or vaginal vault prolapse. Women with high parity; early age at first delivery; menopause; squatting and standing position during delivery; and early return to work after delivery
Miedel/ (40)	2009	Sweden	5489/ (30-79)/ 49.1± 1.5	Researcher- made Ques- tionnaire	48.9	Age and number of delivery were preva- lent risk factors, but there was a signifi- cant relationship with overweight, life- style, family history, constipation
Sliek- ertenhove/ (14)	2009	Poland	1224/ (45-85)/ 59.0± 9.5	Questionnaire UDI, DDI	11.4	Factors that had a significant relationship with POP: Maternal history, occupations with high physical activity In this study, age was not associated with POP



Meta Analysis

Fig. 2: prevalence of pelvic organ prolapse based on physical exam



Meta Analysis

Fig.3: prevalence of pelvic organ prolapse based on questionnaire

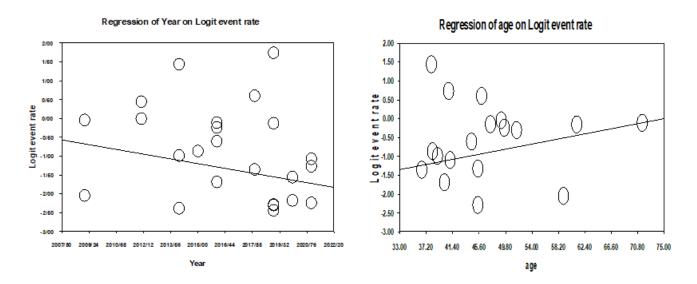


Fig. 4: Meta-regression plot of the prevalence of POP based on year of study and age

Funnel Plot of Standard Error by Logit event rate

Fig. 5: Egger test for assessment of potential publication bias

The probability of publication bias of studies was assessed using Funnel plot with Egger test, and the results were shown in Fig. 5. The results

showed no evidence of any publication bias (P=0.101).

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Discussion

According to the results of this study, the prevalence of POP in women was 28.8%. Various studies reported a great deal of variability in prevalence rates in different countries. This discrepancy in the prevalence rate in different countries can be attributed to the diversity in methodology, such as type of assessment tool (questionnaire or physical examination), the definitions used, age groups, measuring instruments, and ethnicity. Accordingly, a cross-sectional population survey in China by Li et al. reported the prevalence was 9.23%, using PFDI-20 questionnaire for evaluating POP (26), and Direkvand-Moghadam et al. (35) in Iran reported the prevalence was 80.8% by conducting exam-based study for evaluating POP. In addition, in our study, the meta-analysis showed that studies that used questionnaire for diagnosis had a prevalence of 24.8%, and in studies that used physical examination for diagnosis the prevalence was 40.0%, which these estimations are in accordance with other researches. In general, questionnaire-based studies reported lower prevalence and this could be due to a lack of awareness of women and shame in expressing symptoms. Therefore, the affected people are less likely to be diagnosed. Women's awareness of POP is low; this could lead to a lack of reporting and a lack of proper identification of the disease through the questionnaire (41-43). The sensitivity of the prolapse questionnaire to identify cases of pelvic organ prolapse was very low (38.3) even when clearly visible (34). The reason for the difference between the questionnaire and the examination could be also being that many people, who have mild degrees of the prolapse, i.e. less than stage two, do not have annoying symptoms. It should be noted that any prolapse seen in the examination might not cause symptoms, these cases do not require aggressive treatments and it is better to give conservative recommendations.

Regarding to Table 2, the prevalence of POP in the anterior segment was greater (7, 24, 35, 38). Barber et al. also showed a similar result, they stated that prolapse in the anterior segment found twice as often as the posterior segment, and three times more common than apical prolapse (16).

In the present study, the prevalence of POP has declined over the years from 2009 to 2021, which is in contrast to the results of other studies. Several studies predict that the prevalence and incidence of POP will increase in the future (44, 45). Kirby et al. (46) in a study examining the trend of POP from 2000 to 2010 in the United States stated that there was an 85% growth in new patient visits per 1,000 women per year compared with 10 years ago. They predicted from 2010 to 2030, if the population increases by 24%, the demand for care for POP will increase by 35%, Which is 72% more than what they predicted in 2,000. One of the important issues for explaining the increase in POP is the aging of the population, as prolapses are aggravated by age (17). These demographic changes may increase the incidence and prevalence of pelvic floor disorders. The reason for the difference in the outcome of this study with other studies is that other studies have examined the prevalence of POP only for a particular country over time, but the present study investigated the prevalence of POP in different countries, which showed the variety prevalence at different times. It could be explained by differences in racial, genetic, socioeconomic status, and cultural factors.

The present study showed that the prevalence was associated with an increase in age, which is consistent with other studies (30, 47). Hormonal changes, menopause, and changes in the strength of the ligaments can play a role in increasing POP with age (48). Demographic changes such as increasing life expectancy and the elderly population require increasing attention to the future planning of women's health services (49).

Information on the prevalence of pelvic organ prolapse is critical to understanding the public health burden of this condition. In addition, knowledge of the prevalence of POP provides useful information about the need to proactively address these symptoms in patients and to educate healthcare providers in the management of

this disorder. The fact that comparatively few people seek help for their symptoms is problematic, and even when patients do seek help, they are likely to seek help for their most important and bothersome pelvic floor symptom and remain silent about other possible symptoms, which in turn reinforces the important role of the caregiver. Considering the higher prevalence rate of POP on physical examination, it is recommended that pelvic examination be considered in its diagnosis.

Performing meta-analysis with illustrating forest plots, summarizing quantitatively the results of each study, combining the results of various studies, providing a general interpretation of the results, and presenting a general result from studies be among the strengths of the present study. This study like other studies has some limitations. High heterogeneity among the studies, mostly considering the methodologies, definition of POP, and a variety of measurement tools they used, was one limitation of our study. Since most studies have been conducted community-based, the studies' populations were very different. The age range of women was also different. Some studies were conducted with interviews and completion of the questionnaire, and some with a clinical examination. Only six of the 14 studies that used the questionnaire were copies of agreed internationally versions of questionnaires and others used non-standard ones. Therefore, interpreting the results should be done with caution. Future studies with better-defined methodologies, Standardized definitions which suggested by the International prolapse Association, including the population of representatives and similar age groups, and standard assessment tools are needed.

Conclusion

The overall worldwide prevalence of POP in women was 30.9%. POP is silent and people do not express it because of their shame and some of them are asymptomatic, but it has adverse effects on health status and quality of life. Precise

information on prevalence of POP could help clinicians and policy makers to plan for suitable interventional programs (Prevention and proper education) that decrease the prevalence of POPs. Considering the higher prevalence rate of POP based on physical examination, it is recommended that pelvic examination to be considered in its diagnosis. POP should be considered as a health and social problem by health care providers.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors report no conflicts of interest

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