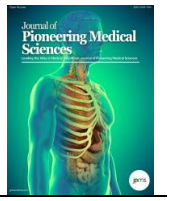
Journal of Pioneering Medical Sciences
Received: September 06, 2024 **Accept**: October 23, 2024 **Publish**: November 04, 2024.
Volume 13, Issue 6, Pages 126-132

DOI https://doi.org/10.61091/jpms2024130615



Prevalence of Symptoms of Bladder Pain Syndrome/Interstitial Cystitis Among Adult Females in the Saudi Arabia

Sulaiman Almutairi
Department of Surgical subspecialty, College of Medicine, Majmaah University, Al-Majmaah 11952, Saudi Arabia
Corresponding author: Dr. Sulaiman Almutairi (e-mail: sa.almutairi@mu.edu.sa).

Abstract: ***Introduction*:** Bladder pain syndrome/interstitial cystitis (BPS/IC) is characterized by repeated pain, pressure, or discomfort in the bladder and pelvic area, and presents both diagnostic and therapeutic challenges for clinicians and researchers because of its enigmatic and poorly comprehended nature. The purpose of this study was to identify the prevalence of bladder pain syndrome/interstitial cystitis in a tertiary care center in the Central region of Saudi Arabia. ***Methodology of the study:*** The study shall be a cross-sectional survey conducted at King Khalid Hospital, Majmaah, Saudia Arabia from May 2021 to April 2024. A total of 800 patients were studied, which included females aged 18 years and above. Data collection was based on patient questionnaires plus some clinical evaluations. The Interstitial Cystitis Symptom Index (ICSI) questionnaire, a validated and widely used tool, was used to assess symptoms associated with Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC). ***Results*:** A significant majority, 57.6%, reported never experiencing a sudden urge to urinate, while 14.1% felt this urge almost always. Regarding frequent urination, 27.6% of the participants never had to urinate within two hours of their last visit, but for 13.9%, this happened almost always. Bladder pain or pressure caused no problems for 62.6% of the respondents, while 11.9% reported this as a moderate problem, and 7.0% thought it was a big problem. The most common comorbidities were anxiety and depression, each affecting 23.4% of participants, reflecting a significant overlap between psychological distress and BPS/IC. **Conclusion:** It was noted that among patients with BPS/IC, quality of life was greatly affected, symptom severity was highly variable, and there was a high prevalence of associated comorbidities of anxiety, depression, and BPS.

Keywords: Bladder, Pain, Interstitial, Patients, Urination, Anxiety.

INTRODUCTION

Bladder Pain Syndrome (BPS), often referred to as Interstitial Cystitis (IC), is a chronic urological condition that affects millions of individuals worldwide. Described by recurrent pain, pressure, or discomfort in the bladder and the pelvic region, BPS/IC is a syndrome that not only poses diagnostic and therapeutic problems for clinicians and researchers due to its elusive and poorly understood nature but also dramatically alters the lives of those who are diagnosed with this disorder [1]. Urinary urgency and frequency are common complications of BPS/IC and these complications can become physically as well as emotionally tiring which consequently causes a lower quality of life. A major difficulty affecting the management of BPS/IC is their defining as the prevalence of the diseases significantly differs depending on the selected population samples, the criteria of diagnosis used in the study, as well as the research methods applied [2]. The prevalence ranges from as low as 6% to as high as 12% which points to the fact that this condition is hard to diagnose. One of the factors that have contributed to these disparities is the absence of a codified definition of BPS/IC, which has resulted in disparate diagnostic approaches [3,4]. Nevertheless, studies have identified that BPS/IC also exists in men but it is less diagnosed cause of male patients are generally diagnosed with chronic prostatitis. Thus, the fact of gender differences in this respect demonstrates that further studies of the causes of this disease and its manifestations depending on demographic factors are necessary [5,6].

The epidemiology of BPS/IC has been established to show considerable geographical differences. BPS/IC has been reported more frequently in the Western countries and the epidemiology of this condition has also been investigated in detail in these regions. For instance, experts approximate that in USA only 3 to 8 million women and 1 to 4 million men might be suffering from BPS/IC [7]. Another similar trend is seen in European countries; as with a Finnish study that showed prevalence ranging one percent. 2% for women of the age 18 to 79 years. These statistics show that BPS/IC can be a significant cost concern and given that many people are still not diagnosed correctly or diagnosed with similar urological and/or gynecological conditions [8]. There is not enough information about BPS/IC from Asian countries, but the available data indicate that the

prevalence of BPS/IC might be lower in Asians. For instance, the research carried out in Japan and Korea shows lower rates as compared to those of the western world [9]. However, these are not necessarily due to the real differences in prevalence of such diseases but could be due to differences in awareness, in diagnosing the diseases and culture in general acceptance of chronic pain. The reasons for the differences in BPS/IC incidence include the differences in diagnostic criteria, the level of patients' awareness, and the availability of medical care [10]. Diagnostic criteria of BPS/IC have been changing throughout the years with initial emphasis given to strictly defined cases with characteristic cystoscopic appearance, namely Hunner's lesion. However, current definitions included a wider range of symptoms and included non-ulcerative forms of BPS/IC making prevalence rate in recent studies to be higher. Self-reporting and patient awareness is also widely used in prevalence studies as well [11]. Described at times as a 'masquerader' – BPS/IC is frequently under-diagnosed specifically because of the symptoms related to chronic pelvic pain [12]. This underreporting distorted the prevalence of skewed data especially among the developing countries where the patients with these diseases do not get easy access to health facilities and in general BPS/IC where little or no awareness exists. As to the etiology of the condition, there are many theories, but the experimental research has not produced consistent results and medication is often not helpful [13]. Hence, BPS/IC is a clinicopathological diagnosis that entails consideration of patients' symptoms. Prior efforts to estimate BPS/IC prevalence have employed method such as, chart review of convenience samples, self-administered newsletters mailed to convenience samples of patients, medical records review, area probability sampling in a restricted geographic area and mail survey on a small probability sample of the population [14]. This study was carried out with the objective to determine the of bladder pain syndrome / interstitial cystitis symptoms among women attending tertiary care hospital in central region of Saudi Arabia.

MATERIALS AND METHODS

Study design and setting

This cross-sectional study was conducted at King Khalid Hospital, Majmaah, Saudi Arabia from May 2021 to April 2024. The study included 800 patients, comprising females aged 18 years and above.

Inclusion and exclusion criteria

Female participants who have experienced chronic pelvic pain, urinary urgency, and frequency for at least six months without any identifiable infection or other clear cause were included in the study. Patients with active urinary tract infections, bladder cancer, or any other diagnosed condition that could account for their symptoms were excluded.

Sample size calculation

The sample size was calculated using the following formula for cross-sectional studies, facilitated by Raosoft software used for calculating sample size formulas in population-based studies (http://www.raosoft.com/samplesize.html):

$n = (Z^2 * \sigma^2) / E^2$

where:

n = sample size
Z = Z-score corresponding to the desired confidence level (95% confidence level, Z = 1.96)
σ = standard deviation of the population (unknown, assumed to be 0.5)
E = margin of error (5%)

Using a prevalence of BPS/IC of 10% (based on previous studies), the estimated sample size was:

$n = (1.96^2 * 0.5^2) / 0.05^2$
$n \approx 785.44$

Rounding up to the nearest whole number, the sample size was set at 800 participants.

Data collection instrument

Data were collected through a combination of patient questionnaires and clinical evaluations. The Interstitial Cystitis Symptom Index (ICSI) questionnaire, a validated and widely used tool, was used to assess symptoms associated with Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC). The ICSI questionnaire, created by the Interstitial Cystitis Association, is a proven tool in assessing the severity and burden of BPS/IC in patients (https://www.baus.org.uk/_userfiles/pages/files/Patients/Leaflets/IC%20symptom%20score.pdf).

Questionnaire design

The ICSI survey has eight questions, broken down into two parts. The initial portion has 4 questions, they all deal with how often, how bad, and how long urinary and pelvic pain symptoms have been present.

- How often have you felt the strong need to urinate with little or no warning?
- Or have you ever gone to urinate less than 2 hours after you just finished peeing?
- How often did you, most typically, get up at night to urinate?
- Have you experienced pain or burning in your bladder?

0-5 scale for each question, the higher the score the worse the symptoms.

The second part is about how much the symptoms affect everyday life, and there are 4 questions.

- Frequent urination during the day?
- Getting up at night to urinate?
- Need to urinate with little warning?
- Burning pain, discomfort, or pressure in your bladder?

Each question is rated on a scale of 0-4, with higher scores indicating more severe symptoms.

Data collection procedure

Participants completed the ICSI questionnaire during their hospital visit, with trained healthcare professionals available to assist with any questions or clarifications, ensuring accurate data collection and minimizing the risk of misinterpretation. Reliability was checked using Cronbach's alpha of 0.87 and is an indicator of high internal consistency, along with establishing validity for the variables being targeted properly.

Statistical analysis

Data were analyzed using SPSS v27.0. Mean and standard deviation were estimated for quantitative variables. Frequencies and percentages were calculated for qualitative variables the statistical significance was set at $p < 0.05$. Descriptive statistics summarized demographic data, and a multivariate regression analysis examined the associations between age (dependent variable) and urinary symptoms that included urgency to urinate and nocturnal episodes and IBS status (independent variables). To corroborate these findings and test the robustness of our results, sensitivity analyses were conducted in which subgroups with potentially significant comorbid conditions, such as anxiety and depression or other psychiatric conditions, were excluded from the analysis.

RESULTS

Data were collected from 800 participants. A significant majority, 57.6%, reported never experiencing a sudden urge to urinate, while 14.1% felt this urge almost always. When it came to frequent urination, 27.6% of respondents never had to urinate within two hours of their last visit, but 13.9% experienced this almost always. Night-time urination was common, with 39.6% waking up once per night and 27.6% not waking at all. Regarding pain or burning in the bladder, 55.8% of participants never experienced these symptoms, while 20.9% reported it sometimes, and 16.4% experienced it several times as presented in Table 1.

Table 1: Interstitial Cystitis (IC) Symptoms Index

Questions	Response	Frequency	Percent
Over the past month, how many times have you felt the urge to urinate suddenly?	Never at all	461	57.6
	Less than once in five times	133	16.6
	Less than half the time	55	6.9
	About half the time	19	2.4
	More than half the time	19	2.4
	Almost always	113	14.1
Over the past month, have you had to urinate less than two hours after you finished urinating?	Never at all	221	27.6
	Less than once in five times	222	27.8
	Less than half the time	115	14.4
	About half the time	38	4.8
	More than half the time	93	11.6
	Almost always	111	13.9
Over the past month, how many times have you woken up at night to urinate?	Never	221	27.6
	One time	317	39.6
	Twice	150	18.8
	Three times	56	7.0
	Four times	38	4.8
	Five times or more	18	2.3
Over the past month, have you had pain or burning in your bladder?	Never at all	446	55.8
	Sometimes	167	20.9
	Several times	131	16.4
	Usually	38	4.8
	Almost always	18	2.3

Frequent urination during the day was not a problem for 46.6% of participants, but 25.9% reported it as a small problem, and 9.3% as a moderate issue. Nighttime urination posed no problem for 56.0% of respondents, yet 11.6% found it moderately troublesome. Sudden urges to urinate were generally not problematic, with 58.0% reporting no issues, though 21.1% experienced it as a very small problem. Bladder pain or pressure caused no issues for 62.6% of participants, but 11.9% reported moderate problems, and 7.0% considered it a significant issue as it shown in table 2.

Table 2: Interstitial Cystitis (IC) Problem Index

How to Cite: Almutairi, Sulaiman. "Prevalence of Symptoms of Bladder Pain Syndrome/Interstitial Cystitis Among Adult Females in Saudi Arabia." *Journal of Pioneering Medical Sciences*, vol. 13, no. 6, 2024, pp. 126-132. DOI: https://doi.org/10.61091/jpms2024130615

Questions	Response	Frequency	Percent
Over the past month, how much frequent urination during the day has caused you a problem?	Never	373	46.6
	Very small problem	109	13.6
	Small problem	207	25.9
	Moderate problem	74	9.3
	Big problem	37	4.6
Over the past month, how much waking up at night to urinate has caused you a problem?	Never	448	56.0
	Very small problem	147	18.4
	Small problem	75	9.4
	Moderate problem	93	11.6
	Big problem	37	4.6
Over the past month, how much did you need to urinate suddenly and cause you a problem?	Never	464	58.0
	Very small problem	169	21.1
	Small problem	73	9.1
	Moderate problem	57	7.1
	Big problem	37	4.6
Over the past month, how much burning, pain or pressure in your bladder has caused you a problem?	Never	501	62.6
	Very small problem	148	18.5
	Small problem	0	0.0
	Moderate problem	95	11.9
	Big problem	56	7.0

Anxiety and depression were the most common comorbidities, affecting 23.4% of participants, highlighting a significant overlap between psychological distress and BPS/IC. Thyroid diseases were present in 9.5% of the population, followed closely by hypertension at 9.3% and diabetes at 9.0%. Heart disease was less prevalent, affecting only 2.4% of participants (Table 3).

Table 3: Comorbidities

Comorbidities	Frequency	Percent
Diabetes	72	9.0
Hypertension	74	9.3
Thyroid diseases	76	9.5
Heart disease	19	2.4
Anxiety and depression	187	23.4

About 30.1% of participants reported not suffering from IBS, 39.8% struggled with it on some days, and 18.5% experienced symptoms more than half the days. Notably, 11.6% of participants reported always dealing with IBS symptoms. These results indicate a strong comorbidity between BPS/IC and IBS, suggesting that a substantial number of patients with bladder pain syndrome also face gastrointestinal challenges, which may further complicate their overall health and quality of life (Table 4).

Table 4: Do you suffer from irritable bowel syndrome (abdominal pain and gas, diarrhea and constipation, fatigue and body fatigue?

Irritable bowel syndrome	Frequency	Percent
I don't suffer	241	30.1
I struggle some days	318	39.8
More than half the days	148	18.5
Always	93	11.6
Total	800	100.0

The Interstitial Cystitis Symptom Index (ICSI) had a mean score of 5.10, with a standard deviation of 4.44, indicating a wide variation in symptom severity across the population. The median ICSI score was 3.00, with an interquartile range (IQR) of 2.0 to 7.0, and scores ranged from 0 to 19. The Interstitial Cystitis Problem Index (ICSPI) had a lower mean score of 3.64 and a standard deviation of 4.35, with a median score of 2.00 and an IQR of 0.0 to 6.0, suggesting variability in the perceived impact of symptoms on daily life. The participants' ages showed a mean of 38.30 years, with a standard deviation of 10.53, a median of 36.00 years, and an IQR of 31.0 to 45.0 years, with ages ranging from 20 to 70 years (table 5).

Table 5: Interstitial Cystitis (IC) Symptoms Index Score and Interstitial Cystitis (IC) Problem Index Score Statistics

PARAMETER	Mean	Std. Deviation	Median	IQR	Minimum	Maximum
ICSI_SCORE	5.10	4.44	3.00	(2.0-7.0)	0	19
ICSPI_SCORE	3.64	4.35	2.00	(0.0-6.0)	0	16
Lifetime	38.30	10.53	36.00	(31.0-45.0)	20	70

The regression analysis indicated that the further along a participant reported being towards having a rising urge to urinate, the more the predicted age decreased (Table 6). On the contrary, the strength of waking up at night to urinate and increased severity of IBS symptoms was positively correlated with the increase in a predicted age. These correlations were statistically significant, indicating a strong association between these urinary symptoms, IBS severity, and age in the population studied.

Table 6: Multivariate Regression Results

Variable	Coefficient	p-value
Intercept	27.11	0.001
Urge to urinate	-4.41	0
Waking up at night to urinate	6.18	0

In the sensitivity analysis (Table 7), after excluding participants with comorbidities, the results showed that the associations between urinary symptoms, IBS severity, and age remained statistically significant. As the urge to urinate increased, the predicted age decreased. Conversely, more frequent nighttime urination and higher IBS severity were still associated with an increase in age. The overall effect sizes were slightly reduced compared to the original analysis, but the relationships remained consistent.

Table 7: Sensitivity Analysis Results

Variable	Coefficient	p-value
Intercept	25.85	0
Urge to urinate	-2.65	0
Waking up at night to urinate	5.17	0

DISCUSSION

The results of the survey showed that the respondents had mild to severe symptoms and the level of urinary symptoms and bladder discomfort varied sharply. The Intercultural Cystitis Symptom Index (ICSI) and Intermittent Cystitis Problem Index (ICSPI) show variation in the BPS/IC sufferers. The mean ICSI score, of 10 respectively and ICSPI score of 3. 64 show that, although some cases reveal a low level of manifested pathology, others include more serious difficulties [15]. This range of results witnessed by standard deviation and interquartile range is further emphasized by the symptoms' variability and the extent of the patient's daily life impairment [16]. The relatively low median indicates that quite a significant part of individuals might get signs that are hardly severe from the perspective of a high index. Nevertheless, the detection of some outliers suggests that BPS/IC can be extremely incapacitating for some people [17]. The results of the study on urinary symptoms are consistent with the previous research on BPS/IC; this study also demonstrated that, in patients with BPS/IC, present symptoms include urinary urgency, frequency, and nighttime urination. Despite 46.2% of participants indicating that they hardly ever experienced a decreased amount of urine passed at night, 6% said it was never an issue in their lives. 9% described it as a very small issue 5%, a moderate problem 22%, and a large issue 9%. Six percent of respondents said that they had a moderate issue with it while 3% labeled it as a minor one [18]. The mean ICSI score of 5.10 and ICSPI score of 3.64 indicate that while some participants experienced mild symptoms, others faced more severe challenges. The broad range of scores, as indicated by the standard deviations and interquartile ranges, reflects the heterogeneity in symptom presentation and the degree to which these symptoms interfere with daily life. The lower median scores suggest that a substantial portion of the population might experience symptoms that, although present, are not overwhelmingly severe [19]. However, the presence of extreme scores underscores the debilitating nature of BPS/IC for a subset of patients. The study's findings on urinary symptoms align with existing literature on BPS/IC, where symptoms such as urinary urgency, frequency, and nighttime urination are prevalent. Despite 46.6% of participants reporting that frequent daytime urination was never a problem, a significant proportion, 25.9%, found it to be a small problem, and 9.3% rated it as a moderate problem. Similarly, nighttime urination did not pose a problem for 56.0% of respondents, but 11.6% found it moderately troublesome [20]. This suggests that all these conditions are mutually reinforcing and they result in increased symptom burden which hampers the treatment process and minimizes the quality of life of such patients. The fact that the age ranged from 20 to 70 years of age also depicts that even young people are at risk of BPS/IC, therefore requiring age-sensitive management [21]. This study has some limitations also. First, its cross-sectional design restricts the ability to infer causality between BPS/IC and comorbid conditions like anxiety or IBS. Second, potential selection bias may exist, as participants were drawn from a specific population, which could limit the generalizability of the findings. Third, reliance on self-reported data introduces the risk of recall bias, potentially affecting the accuracy of the responses.

CONCLUSION

It is concluded that bladder pain syndrome/interstitial cystitis (BPS/IC) significantly impacts a subset of women attending tertiary care, with varying degrees of symptom severity and associated comorbidities such as anxiety, depression, and IBS. The study highlights the significant variability in BPS/IC symptoms and their impact on daily life. The high prevalence of comorbid conditions, particularly anxiety, depression, and IBS, suggests that BPS/IC is part of a broader syndrome that requires comprehensive management.

Data availability

The data supporting this study's findings are

available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Institutional Review Board statement

This study was approved by the institutional review board of the Deanship of Scientific Research at Majmaah University with IRB No. 20-270E dated May 2020.

Informed consent statement

Consent was obtained rom the participants before they were enrolled in thew study.

Authors' contributions

Conceptualization, Methods, Data collection, Data analysis, Manuscript write up and review was done by Suleman Almutairi

Funding

Not funded

Acknowledgments

I would like to thank the Director of King Khalid Hospital for helping us to conduct this study.

REFERENCES

1. Doggweiler, R., et al. "A Standard for Terminology in Chronic Pelvic Pain Syndromes: A Report from the Chronic Pelvic Pain Working Group of the International Continence Society." Neurourology and Urodynamics 36.4 (2017): 984-1008. https://doi.org/10.1002/nau.23072.
2. Malde, S., et al. "Guideline of Guidelines: Bladder Pain Syndrome." *BJU International* 122.5 (2018): 729-743. https://doi.org/10.1111/bju.14399.
3. Kumar, P., et al. "Bioenergetic Profiles of Peripheral Mononuclear Cells and Systemic Inflammation in Women with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS)." PLOS ONE 19.2 (2024): e0298981. https://doi.org/10.1371/journal.pone.0298981.
4. Clemens, J. Q., et al. "Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome." Journal of Urology 208.1 (2022): 34-42. https://doi.org/10.1097/JU.0000000000002756.
5. Kowalczyk, P., et al. "Mitochondrial Oxidative Stress—A Causative Factor and Therapeutic Target in Many Diseases." International Journal of Molecular Sciences 22.24 (2021): 13384. https://doi.org/10.3390/ijms222413384.
6. Akiyama, Y. "Biomarkers in Interstitial Cystitis/Bladder Pain Syndrome with and without Hunner Lesion: A Review and Future Perspectives." Diagnostics 11.12 (2021): 2238. https://doi.org/10.3390/diagnostics11122238.
7. Lin, H. Y., et al. "Urinary Biomarkers in Interstitial Cystitis/Bladder Pain Syndrome and Its Impact on Therapeutic Outcome." Diagnostics 12.1 (2021): 75. https://doi.org/10.3390/diagnostics12010075.
8. Webster, J. D., and D. Vucic. "The Balance of TNF Mediated Pathways Regulates Inflammatory Cell Death Signaling in Healthy and Diseased Tissues." Frontiers in Cell and Developmental Biology 8 (2020): 365. https://doi.org/10.3389/fcell.2020.00365.
9. Apaijai, N., et al. "Cognitive Impairment Is Associated with Mitochondrial Dysfunction in Peripheral Blood Mononuclear Cells of Elderly Population." Scientific Reports 10.1 (2020): 21400. https://doi.org/10.1038/s41598-020-78551-4.
10. Ajaz, S., et al. "Mitochondrial Dysfunction as a Mechanistic Biomarker in Patients with Non-Alcoholic Fatty Liver Disease (NAFLD)." Mitochondrion 57 (2021): 119-130. https://doi.org/10.1016/j.mito.2020.12.010.
11. Patnaik, S. S., et al. "Etiology, Pathophysiology and Biomarkers of Interstitial Cystitis/Painful Bladder Syndrome." Archives of Gynecology and Obstetrics 295 (2017): 1341-1359. https://doi.org/10.1007/s00404-017-4364-2.
12. Willig, A. L., et al. "Monocyte Bioenergetic Function Is Associated with Body Composition in Virologically Suppressed HIV-Infected Women." Redox Biology 12 (2017): 648-656. https://doi.org/10.1016/j.redox.2017.04.005.
13. Berry, S. H., et al. "Prevalence of Symptoms of Bladder Pain Syndrome/Interstitial Cystitis among Adult Females in the United States." The Journal of Urology 186.2 (2011): 540-544. https://doi.org/10.1016/j.juro.2011.03.132.
14. Mendonça, F. T., et al. "Effect of Ondansetron on Spinal Anesthesia-Induced Hypotension in Non-Obstetric Surgeries: A Randomised, Double-Blind and Placebo-Controlled Trial." Brazilian Journal of Anesthesiology 71 (2021): 233-240. https://doi.org/10.1016/j.bjane.2020.12.028.
15. Sheng, Z. M., et al. "Comparative Dose-Response Study on the Infusion of Norepinephrine Combined with Intravenous Ondansetron versus Placebo for Preventing Hypotension during Spinal Anesthesia for Cesarean Section: A Randomised Controlled

Trial." International Journal of Surgery 110.2 (2024): 832-838. https://doi.org/10.1097/JS9.0000000000000920.

16. Aksoy, M., et al. "Granisetron or Ondansetron to Prevent Hypotension after Spinal Anesthesia for Elective Cesarean Delivery: A Randomized Placebo-Controlled Trial." Journal of Clinical Anesthesia 75 (2021): 110469. https://doi.org/10.1016/j.jclinane.2021.110469.
17. Mohamed, S., et al. "Effectiveness of Prophylactic Ondansetron in Preventing Spinal Anesthesia Induced Hypotension and Bradycardia in Pregnant Mother Undergoing Elective Cesarean Delivery: A Double Blinded Randomized Control Trial." International Journal of Surgery Open 35 (2021): 100401. https://doi.org/10.1016/j.ijso.2021.100401.
18. Zhang, Y., et al. "Intravenous Ondansetron for the Prevention of Supine Hypotensive Syndrome during Spinal Anesthesia for Cesarean Section: A Randomized Controlled Trial." Frontiers in Pharmacology 15 (2024): 1194196. https://doi.org/10.3389/fphar.2024.1194196.
19. Sharma, S. N., and G. S. Maravi. "Effect of Ondansetron in Prevention of Hypotension in Elective Lower Segment Cesarean Section under Spinal Anesthesia: A Randomized, Double-Blind Study." International Journal of Scientific Study 7.11 (2020): 89-98.
20. El-Rahman, A., et al. "Evaluation of the Efficacy of Ondansetron in Preventing Post Spinal Anesthesia Hypotension in Cesarean Sections." Benha Journal of Applied Sciences 8.8 (2023): 43-50. https://doi.org/10.21608/bjas.2023.228234.1225.