

## The Prevalence of Nocturnal Enuresis among Iranian Children: A Systematic Review and Meta-Analysis

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**Purpose:** Nocturnal enuresis is one of the most common diseases in children, which can affect their mental health. The aim of the present study is to determine the prevalence of nocturnal enuresis in Iranian children through systematic review and meta-analysis.

**Materials and Methods:** The present study was conducted through systematic review and meta-analysis of studies during March 2000- July 2018. Articles related to the subject were reviewed by searching the Medline (PubMed), Scopus, ScienceDirect, SID, Magiran, Barakat, and Google Scholar databases where the heterogeneity of studies was investigated using I<sup>2</sup> index. The data analysis was then carried out using Comprehensive Meta-Analysis software.

**Results:** 15 articles with a sample size of 16614 individuals aged 3 to 18 years entered the meta-analysis process. The overall prevalence of nocturnal enuresis in children of Iran was 10.2% (95% CI: 7-14.8%). The highest and lowest prevalence of nocturnal enuresis was seen in children living in Tehran 28.5% (95% CI: 16.1% -45.4) and Tabriz 1.8% (95% CI: 1.2-2.8%), respectively. The findings of the present study revealed that the prevalence of nocturnal enuresis in children decreases with enlargement of the sample size. In addition, the prevalence of nocturnal enuresis grows with an increase in the years of research, which is statistically significant ( $P < 0.05$ ).

**Conclusion:** Considering the high prevalence of nocturnal enuresis in the current study, health policy makers need to raise the awareness of families by taking efficient and effective policies.

**Keywords:** nocturnal enuresis; prevalence; children; Iran; meta-analysis

### INTRODUCTION

Children are the architects of the society's future, so their physical and mental health status is important and their disorders and diseases should be taken care of seriously<sup>(1)</sup>. Children who are neglected physically and psychologically today and have no access to adequate health and education will be individuals with physical and mental disabilities in the future<sup>(2)</sup>. Nocturnal enuresis is one of the most commonly reported diseases in children following allergic diseases. This disorder is known as involuntary passage of urine during sleep<sup>(3)</sup>, as well as frequent and unintentional passage of urine in the clothes or bed in children who should have gained control over their bladder considering their age. It is also known in case of absence of certain physical abnormalities<sup>(4)</sup>. The majority of children gain regular daytime urine control by age of 3 to 4, so 5 years old is considered as the best age for the diagnosis and screening of the nocturnal enuresis<sup>(5)</sup>. Nocturnal enuresis diagnosis is proved when involuntary urination occurs in clothes or bed at least twice a week for three consecutive months, or the bedwetting manifests itself as a clinically important concern in the child's life<sup>(6)</sup>. Nocturnal enuresis occurs among 3-15% of 6-year-old children at least one night in a month, and reaches 4 to 16% in 12-year-old children<sup>(7)</sup>. Mental health problems

in children with nocturnal enuresis are 2 to 6 times more prevalent than those of the total population of the world<sup>(8)</sup>. Nocturnal enuresis can cause severe mental stress for families and discomfort for children and adolescents. Parents often feel anxious and angry and may blame, punish, and humiliate children due to lack of awareness of this disorder. They may also create serious mental injuries for children<sup>(8,9)</sup>. Diagnostic and therapeutic measures, as well as awareness raising plans in families, require access to comprehensive information and statistics on the prevalence of nocturnal enuresis in children. Studies in Iran have reported different rates of nocturnal enuresis. In a study in Sanandaj in 2001, the prevalence of nocturnal enuresis was 8.8%<sup>(10)</sup>, 14.3% in Ahwaz in 2013<sup>(11)</sup>, and 11.9% in Birjand in 2005<sup>(12)</sup>, indicating the inconsistency and uncertainty of the nocturnal enuresis among Iranian children. There are still unclear statistics at the national level.

The aim of the present study is to determine the overall prevalence of nocturnal enuresis in Iranian children by systematic review and meta-analysis. The results of this study can be useful in conducting interventional studies as well as making health policies.

### MATERIALS AND METHODS

This study was a systematic review and meta-analysis

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**Table 1.** Specifications of studies included in the study

Row	Author (Reference)	Publication year	Area	Participants' Age	Sample size	Prevalence
1	Ghotbi <sup>(11)</sup>	2001	Sanandaj	9.3±9	681	8.8
2	Zargar <sup>(12)</sup>	2013	Ahwaz	5-6	807	14.3
3	Khazaei <sup>(13)</sup>	2005	Birjand	5.5-6.5	455	11.9
4	Haghbin <sup>(14)</sup>	2003	Yasuj and Gachsaran	7	2846	3.6
5	Mohammadpour <sup>(15)</sup>	2012	Gonabad	8.6±1.05	250	6.8
6	Emamghoraiishi <sup>(16)</sup>	2004	Jahrom	6-11	1000	16.5
7	Hakim <sup>(17)</sup>	2015	Ahwaz	8.6±1.8	200	32
8	Naderian <sup>(18)</sup>	2000	Tehran	4-12	35	28.5
9	Shafipour <sup>(19)</sup>	2014	Rasht	7-11	768	7.2
10	Ranjbar <sup>(20)</sup>	2003	Tabriz	5-16	1092	1.8
11	Hashem <sup>(21)</sup>	2013	Urmia	7-11	918	18.7
12	Safarinejad <sup>(22)</sup>	2013	Tehran	5-18	7562	6.8

and has been the result of findings extracted from the previous studies on the prevalence of nocturnal enuresis in Iranian children. It includes articles published in domestic and foreign journals, and searches carried out in SID, Magiran, Barakat Knowledge Network system, Medline (PubMed), ScienceDirect, Scopus, and Google Scholar during March 2000 to July 2018.

### Search strategy

The search process was carried out in the above websites using the keywords of 'nocturnal enuresis', 'children', and their equivalent English words and possible combinations. With regard to the Persian databases, the search was carried out using Farsi keywords of (nocturnal enuresis), (children) while their equivalent English keywords were used in the English key words of nocturnal enuresis, children. In addition, both Farsi and English words were searched in the Google scholar search engine and the (AND) and (OR) operators were combined in order to provide more comprehensive access to all articles. Specifically, OR operators were applied to check the common names for a disorder (Children OR Preschool), (Nocturnal enuresis OR Nighttime Urinary

Incontinence). AND word was used in the keywords by matching words in the MeSH browser.

### Criteria for selecting and evaluating articles

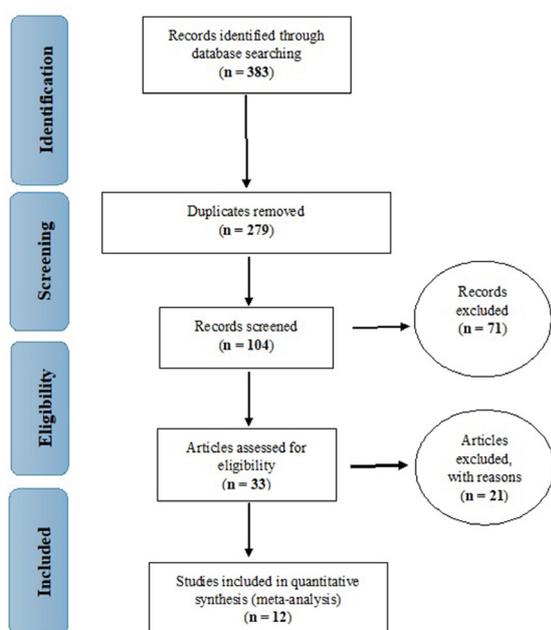
First, all articles were collected using selected keywords and a list of abstracts was then prepared after the search process. After hiding the articles' specifications, including the magazine name and the author's name, the full text of the articles was provided to the reviewers. Each article was read by two reviewers (MM and AVR) independently. If the article was rejected, the reason should have been mentioned. In case of any disagreement between the two reviewers (MM and AVR), the article was judged by a third reviewer (RJ). The inclusion criteria were Persian and English articles taken from cross-sectional studies on the prevalence of nocturnal enuresis in Iranian children in age group of 4-15 years. In order to evaluate the articles obtained in this study, the PRISMA checklist was used. Other studies, including review, case-control, cohort, and interventional studies were excluded from the list of articles. In this study, searching keywords in Google and reviewing related websites were done to examine gray literature, which is the general name for non-formally published scholarly or substantive information. Duplicate publication and multiple publications from the same population would be removed using citation management, software EndNote (version X7, for Windows, Thomson Reuters).

### Quality assessment

For quality assessment of cross-sectional studies, the STROBE checklist was used. This checklist contains 22 sections, 18 of which are general and practical for all observational studies, including cohort, case study, and cross-sectional studies. On the other hand, four sections are specific, depending on the type of study as well as various aspects of the methodology including objectives of the study, determining the appropriate sample size, type of study (cross sectional, case-control and cohort), sampling method, research population, data collection method, variables definition and sample study method, data collection tools, objectives of the study, statistical test, and study results. Accordingly, the maximum quality score of 32 was considered, while papers with a score of less than 14 were considered to have low quality, and thus excluded from the study.

### Statistical analysis

In each study, the prevalence of nocturnal enuresis in children was obtained. The heterogeneity of studies was also assessed using the I<sup>2</sup> index. Overall, the hetero-



**Figure 1.** The flowchart for the stages of including the studies in the systematic review and meta-analysis (PRISMA 2009)

**Table 2.** Effect of effective factors on heterogeneity (Meta-regression)

		Point estimate	Standard Error	Lower limit	Upper limit	P value
Sample Size	slope	-0.0001	0.00001	-0.0001	-0.00009	0.000
	intercept	-1.87	0.04	-1.93	-1.76	0.000
Years	slope	0.08	0.007	0.06	0.09	0.000
	intercept	-163.4	14.4	-191.73	-135.11	0.000

genicity was classified into three categories including I2 value of < 25% (low heterogeneity), 25-75 % (moderate heterogeneity), and >75% (high heterogeneity) (10). The data were analyzed using the Comprehensive Meta-analysis (Biostat, Englewood, NJ, USA version 3). The probability of publication bias in results was measured using the funnel plot, the Egger test, and the significance level of 0.05 along with Begg and Mazumdar's rank correlation and the significance level of 0.1. In addition, the meta-regression test was used in two factors of the sample size and research year to investigate the effects of the potential factors affecting the heterogeneity of the studies.

**RESULTS**

**Search output**

According to the review made on the prevalence of nocturnal enuresis among Iranian children and included articles published in domestic and foreign journals, along with the searches made, 383 articles were obtained from the first search, which was ultimately evaluated based on PRISMA 2009 (Figure 1). Finally, in the final review, relevant articles were introduced into the meta-analysis, in which 12 relevant articles were included, as reported in Table 1. This table presents the researcher's name, the article title, the year, and place of the study, sample size, the frequency, and prevalence of nocturnal enuresis in children in the studies<sup>(11-22)</sup>.

**Heterogeneity and publication bias**

The heterogeneity of the studies was evaluated using the I2 test, was 97%, showing a high heterogeneity in the studies. Therefore, the random effects model was used to combine the results of the studies. The publi-

cation bias of the results was analyzed by a funnel plot and Egger test (Figure 2) at the significance level of 0.05. It indicated that the publication bias was not statistically significant (P = 0.573). Also, considering the high sample size examined in the study, the publication bias was also investigated based on the Begg and Mazumdar's rank correlation test at the significance level of 0.1, which was not statistically significant (P = 0.921).

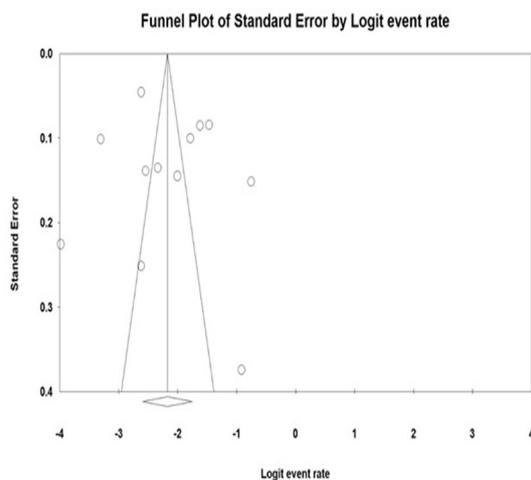
The total sample size of the study was 16614 participants aged 3 to 18 years. The overall prevalence of nocturnal enuresis in Iranian children based on meta-analysis was 10.2% (95% CI: 7-14.8%). The maximum and minimum prevalence of nocturnal enuresis was seen in children living in Tehran 28.5% (95% CI: 16.1%-45.4)<sup>(18)</sup> and Tabriz 1.8% (95% CI: 1.2-2.8%),<sup>(20)</sup> respectively (Figure 3). In this figure, the prevalence of nocturnal enuresis in children is shown based on the random effects model, where the black square indicates the prevalence rate and the length of the line segment, on which the square shows 95% CI of each study. The diamond sign reveals the prevalence rate of nocturnal enuresis in all studies at the national level.

**Sensitivity analysis**

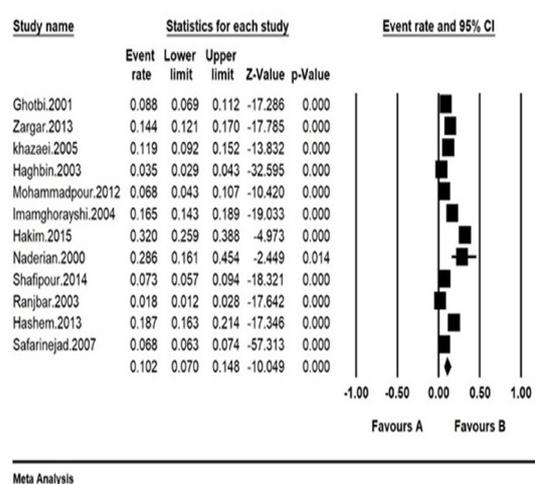
A sensitivity analysis was performed to ensure the stability of results, where after removing each study, the results did not change (Figure 4).

**Meta-regression**

In order to investigate the effects of factors potentially affecting heterogeneity in the prevalence of nocturnal enuresis in children, a meta-regression was used for two factors of sample size and year of study (Table 2). Based on Figure 2, the prevalence of nocturnal enure-



**Figure 2.** Funnel plot for results of prevalence of nocturnal enuresis in Iranian children



**Figure 3.** Overall prevalence of nocturnal enuresis in children based on random effects model

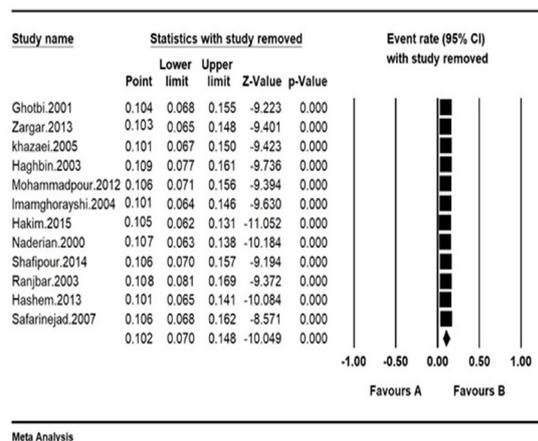


Figure 4. Results of sensitivity analysis

sis diminishes in children with increasing sample size, which is statically significant ( $P < 0.05$ ). It was also found that the prevalence of nocturnal enuresis rose in children with an increase in the number of years, which was statistically significant ( $P < 0.05$ ) (Table 2).

## DISCUSSION

Nocturnal enuresis is one of the most common problems in children, which needs to be treated through counseling and effective measures<sup>(23)</sup> due to its mental and psychological impacts on the child and the subsequent problems for the family. Previous studies have stated that nocturnal enuresis is a multifactorial disorder and cases such as impaired cerebral cortex maturation, rapid eye movement sleep behavior disorder (RBD), disturbed circadian rhythm of ADH secretion, genetic disorders, psychiatric disorders, and kidney problems can contribute to its development<sup>(24,25)</sup>. Many reports have concluded that since the disease prevalence decreases automatically by 14% with increasing age of the child, the delayed development of the nervous system is one of its major etiologies. Other factors such as the socioeconomic status of the family, previous history of urinary tract infection, family history, parental education, and mental status can also contribute to the prevalence of nocturnal enuresis<sup>(26,27)</sup>. Ismail et al.<sup>(28)</sup> reported, in their study in Egypt, that there are other risk factors for this disorder such as positive family history, deep sleep, low socioeconomic levels, and child punishment. Nocturnal enuresis can also follow a family pattern and can usually affect several members in one family<sup>(26)</sup>. Studies have suggested that the nocturnal enuresis in homozygous twins is more common than in heterozygous twins. In the current study and a survey on 16614 children aged 3-18 years, the overall prevalence of nocturnal enuresis in Iranian children was reported to be 10.2% based on a meta-analysis. Studies in the Middle East and Asian countries have reported different prevalence rates as follows: Turkey, 16.2%<sup>(29)</sup>, Saudi Arabia 15%<sup>(30)</sup>, Taiwan 10% (31), Korea 9.2%<sup>(32)</sup>, India 11.1%<sup>(33)</sup>, China 4.3%<sup>(34)</sup>, Australia 18.9%<sup>(35)</sup>. The same studies in European and African countries reported the following prevalence rates: Italy 3%<sup>(36)</sup>, Burkina Faso (13%)<sup>(37)</sup>, Egypt 10.1%<sup>(28)</sup>, and Nigeria 23.2%<sup>(38)</sup>. Differences can be attributed to cultural and geographical differences in studies. In most studies, the prevalence

of nocturnal enuresis has been greater in boys than in girls<sup>(39)</sup>. For example, the results of a study in Spain showed a boy-girl ratio 5:1<sup>(40)</sup>. The results of a study in Saudi Arabia<sup>(30)</sup> also revealed a higher prevalence of nocturnal enuresis in boys; researchers justified it by stating that girls usually reach every step of bladder control faster than boys do, which is due to the early development of bladder control in girls<sup>(41)</sup>. Further studies reported the same prevalence rates for nocturnal enuresis in both genders<sup>(42)</sup>. However, another study, which reported higher prevalence rates for nocturnal enuresis in girls, attributed such results to the higher risk of urinary tract infections (UTIs) in this gender<sup>(43)</sup>. Nocturnal enuresis can be considered as a problem with associated individual, family, social, and emotional dimensions. Considering that this disorder is one of the children's behavioral disorders and various factors are involved in it, the following measures should be considered: increasing family's level of awareness through counseling, adopting health measures as well as appropriate policies to assess the mental health of children, evaluating physical and mental abilities in measurement bases before entering school for early diagnosis and treatment, providing guidance to parents and mental health services in schools and establishing psychological counseling centers, and familiarizing parents with the mental health issues of children in order to adequately identify and deal with children's mental disorders<sup>(13)</sup>. The ultimate goal is to prevent social-functional consequences in children and enhance their self-confidence and promote their physical and mental health status by treating their disorder.

The most important limitation of the present study was the lack of access to the full texts article of some of the old articles and the omission of some of these articles due to their low quality in evaluating the quality of the articles reviewed.

## CONCLUSIONS

Considering the high prevalence of nocturnal enuresis in the current study, it is imperative that health-policy makers take effective and effective measures to raise family awareness, and ensure early diagnosis and treatment.

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## CONFLICT OF INTEREST

There are no conflicts of interest to be disclosed.

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