Research Article

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Prevalence of proteinuria among Iranian children: A systematic Review and meta analysis

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Abstract

Introduction: Screening of kidney diseases by urinalysis in preschool children was approved in many parts of the world with inexpensive tools such as urinary dipsticks. In this study the researchers investigate the prevalence of proteinuria among Iranian children. the aim of this study was to evaluate the prevalence of proteinuria among Iranian children.

Methods: The methods used for this systematic review were based on the "Cochrane Systematic Study Booklet" and "Appropriate Items for Systematic and Meta-Analysis Study (PRISMA)" tool. To find references, the international Databases (MEDLINE PubMed interface), Google Scholar, and Web of Science) and domestic databases (SIDs and Magiran) and journals were searched; unlimited searching, in terms of both setting and language, was done until June 30, 2018.

Results: The final research was conducted on 6840 participants; with an age range of 1 to 14 years old. Meta‑analysis Prevalence of proteinuria among Iranian children Based on the results of random effects model, the Prevalence of proteinuria among Iranian children in 6840 patients was %4.8 (95% confidence interval [CI]: 4.2, 5.5, $I^2 = 97.5\%$).

Conclusion: While the prevalence of asymptomatic proteinuria in various studies in Iran has been widely differentiated, high levels of proteinuria were reported in Iranian children according to the findings of the present study. In order to justify and accurately diagnose the prevalence and causes of asymptomatic proteinuria as a key indication of kidney disease in Iranian children, more detailed studies are required with a larger sample size in all provinces in Iran.

Keywords: children, Iranian, proteinuria

Introduction

Proteinuria is a characteristic of several renal problems and diseases (1). For the first time, Richard Bright showed the relationship between kidney disease and protein excretion in urine (2). Protein exposure to creatinine has a close correlation with 24-hour urine protein values, usually less than 0.2; however, in children less than 2 years of age this ratio is 0.5 (3). Although this symptoms is more evident in Nephrotic syndrome and nephritis, proteinuria is also found to be milder in other types of renal tubular diseases (4). It may also be found in childhood and normal children(5). Based on available evidence, proteinuria is an indicator of kidney disease; however, it is itself a

mechanism that influences the progression of kidney damage (6). Chronic kidney disease is sometimes asymptomatic, and diagnosis and treatment may be delayed which, in turn, causes poor prognosis (7-9). 150 mg per 24 hours is the maximum protein excretion in normal children (10). The results of some studies have shown that annual urine screening can detect chronic renal disease before progression to renal failure(11-13). Increased protein levels also provide the best prediction of progressive kidney damage (14). Early diagnosis of kidney disease in children is important in order to prevent further damage, delay the progression of the disease, reduce the number of

patients with progressive renal failure and reduce mortality and disability (15). There are long-term plans for urinary screening for early detection of renal diseases in some countries and several studies have so far been carried out to confirm the usefulness of this program(16).the aim of this study was to evaluate the prevalence of proteinuria among Iranian children.

Methods

Eligibility criteria

The methods used for this systematic review were based on the "Cochrane Systematic Study Booklet" and "Appropriate Items for Systematic and Meta-Analysis Study (PRISMA)" tool. Observational studies conducted on general population have been added and studies conducted on specific population have been removed. Results are summarized as reported in the research. The minimum sample size was 25 patients in each study. The target population covers the total population of Iranian children who entered the study. Prevalence of proteinuria among Iranian children was calculated in this study.

Searching strategies and databases

The review of references and resources was done using the Medical Subject Headings (MeSH) and keywords related to the source of information on Prevalence of proteinuria among Iranian children. To find references, the international Databases (MEDLINE PubMed interface), Google Scholar, and Web of Science) and domestic databases (SIDs and Magiran) and journals were searched; unlimited searching, in terms of both setting and language, was done until June 30, 2018. PRESS standard and the Health Sciences Librarian were used for designing the strategy. MEDLINE application was used to search other databases. In addition, PROSPERO was used to provide a systematic search that was completed recently. To search for headlines and abstracts, boolean (AND, OR, NOT), mesh, coordinate {truncation} * and related words were used; following keywords were used to provide a comprehensive context: children, Iran,proteinuria .

Research selection and data extraction

According to the research protocol, two researchers observed the titles and abstracts separately according to the eligibility criteria; in the next step, after the removal of repeated studies, the full text of the paper

was studied based on the eligibility criteria and the required information was extracted. Consensus method was used to solve the disagreements between two researchers. The extracted data included the general information (corresponding author, year and place), characteristics of the research (research design, sample size, location, study period, and risk of bias), and characteristics of participants.

Quality control

To assess the quality of the methodology and bias risk, each observation study was evaluated using a tool developed by Hoy et al; this 10-item scale evaluated the quality of the study in two dimensions, including external credentials (items 1 to 4 target populations, sampling frame, sampling method, and minimum indirect neglect) and internal validity (items 5 up to 9 covering methods for data collection, case definition, study tools, and data collection mode and item 10 covering assessing relevant assumptions or analyzes). The risk of abuse was assessed by two researchers separately and possible disparity of ideas was resolved by consensus.

Aggregation of data

All eligible studies were included within the systematic review. The data was combined using forest plot graph; random effects model was used to evaluate Prevalence of proteinuria among Iranian children. The heterogeneity of primary studies was assessed by performing I^2 tests. Meta-analysis was performed using the STATA 14 statistical software.

Results

1. Selecting eligible papers and researches

In the initial search on various databases, a total of 261 articles were reviewed, 232 of which turned out to be repetitive during screening process of title and abstract. 19 articles were removed due to unrelated title; out of the remaining 10 articles, 5 articles met the inclusion criteria. Of the 5articles that were removed, 2 were reviews, 1were letters to editors, 1 had no complete text, and 1 had low quality and could not be considered in the research. (Figure 1)
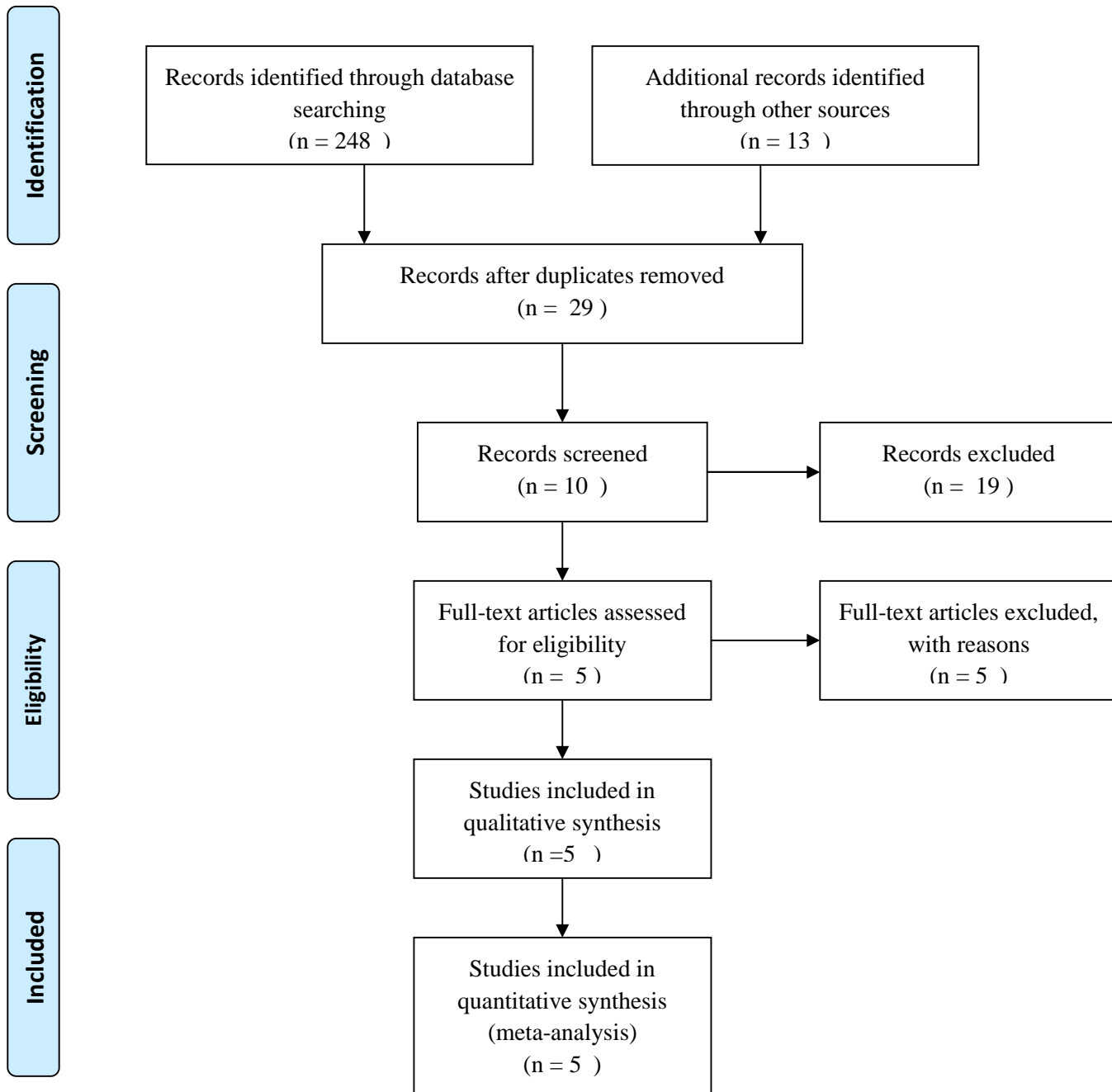
PRISMA 2009 Flow Diagram

Fig. 1 Study selection process

2. Characteristics of the researches and papers

The final research was conducted on 6840 participants; with an age range of 1 to 14years old; a cross-sectional design was used in all studies.

Research was conducted in only 5 provinces out of 31 provinces of Iran. Of the 5 studies , one was from Yazd , one from Isfahan , One from Ghazvin, one from Zahedan and one from Rasht. Required data was collected through interview (n = 5) and most of the studies had a low bias risk (n = 4) (Table 1).

Table 1: Characteristics of final included studies about Prevalence of proteinuria among Iranian children

ID	Author	Year	N	City	Prevalence	Bias
1	Dalirani[21]	2009	659	Gazvin	0.01/8	Low
2	Sadeghi[22]	2008	1169	Zahedan	0.07	Low
3	Badeli[23]	2009	1520	Rasht	0.05/8	Low
4	Jari[24]	2018	478	Isfahan	0.25/9	Moderate
5	Jafari[25]	2015	3014	Yazd	0.01/79	Low

Meta-analysis Prevalence of proteinuria among Iranian children :

Based on the results of random effects model, the Prevalence of proteinuria among Iranian children in 6840 patients was %4.8 (95% confidence interval [CI]: 4.2, 5.5, I^2 = 97.5%) (table 2) .

Table 2: Prevalence of proteinuria among Iranian children

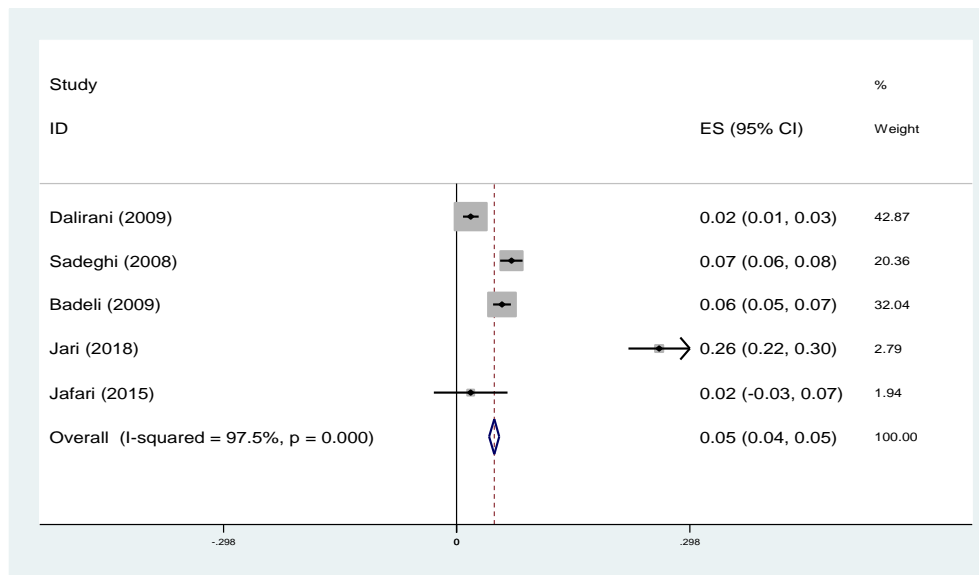| Study	Year	ES	95% conf. Interval		%weight
			Low	Up	
Dalirani	2009	0.018	0.008	0.028	42.87
Sadeghi	2008	0.070	0.055	0.085	20.36
Badeli	2009	0.058	0.046	0.070	32.04
Jari	2018	0.259	0.22	0.298	2.79
Jafari	2015	0.018	-0.029	0.065	1.94
Pooled ES	--------	0.048	0.042	0.055	100

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Fig. 2 : The Prevalence of proteinuria among Iranian children and its 95% interval for the studied cases according to the year and the city where the study was conducted based on the model of the random effects model. The midpoint of each section of the line estimates the% value and the length of the lines showing the 95% confidence interval in each study. The oval sign shows Prevalence of proteinuria among Iranian children for all studies.
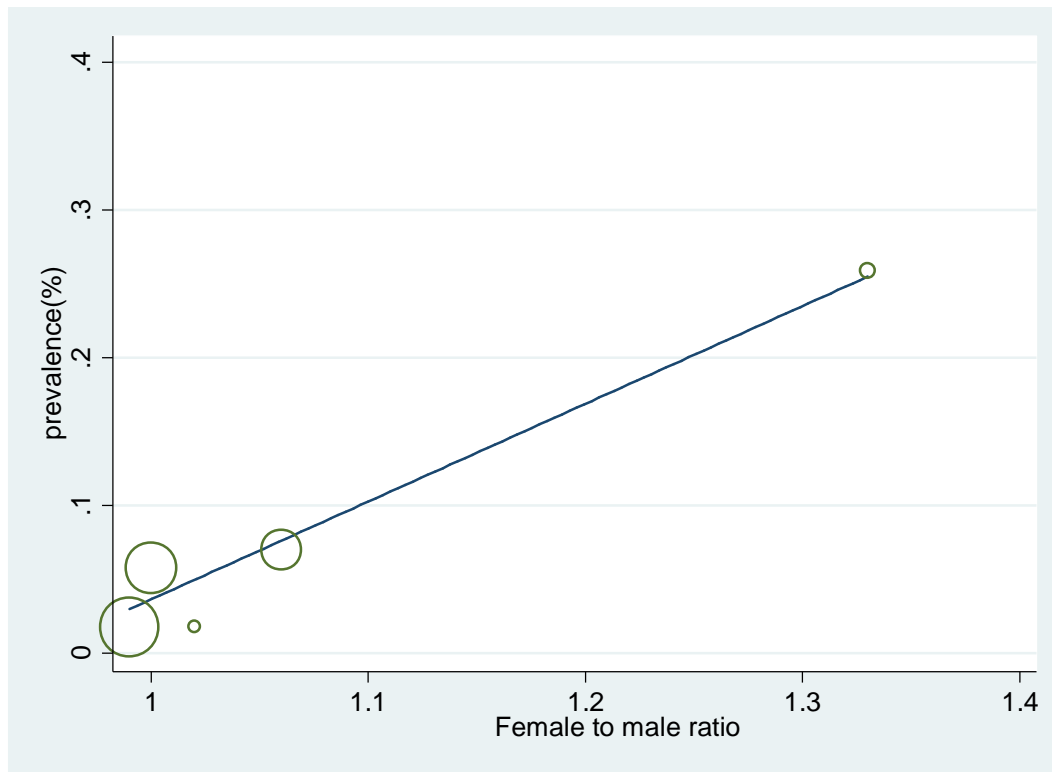

FIG. 4. Meta-regression between the female-to-male ratio and the Prevalence of proteinuria among Iranian children

Discussion and Conclusion

The excretion of protein in the urine, or proteinuria, often occurs when glomeruli or tubules are damaged in the kidneys[17]. Inflammation or glomerular ulcers can increase the amount of protein and, sometimes, red blood cells in the urine[18]. Damage to tubules can prevent reabsorption of protein[19]. Protein excretion from the kidney may also occur when there is a very large amount of a small protein in the blood and tubules cannot absorb all of the existing amount[20]. Although very low levels of protein in the urine can be considered normal, the detection of high amount of protein in the urine can be a sign of early damage to the kidneys, which, if not controlled, can be a factor in further damage to the kidneys. Over time, it can lead to kidney failure, dialysis, or kidney transplant. Diagnosis and timely treatment of the main cause of protein excretion in the urine can reduce or curb the progression of renal failure.

Based on our research the Prevalence of proteinuria among Iranian children in 6840 patients was %4.8 (95% confidence interval [CI]: 4.2, 5.5, $I^2 = 97.5\%$) .

Limitations

One of the limitations of the present study is the small number of studies conducted on the Prevalence of proteinuria among Iranian children. However, as long as the present researchers can claim, the present principled revision and statistical analysis has been the first attempt to evaluate the Prevalence of proteinuria among Iranian children. Another limitation of this study is the inclusion of only 5 provinces out of 31 provinces of Iran, a fact which makes it difficult to generalize the results. Although investigators kept cautious of writers, institutes, journals and other related information, two independent reviewers supervised the selection of related papers and the third reviewer solved all the and possible disagreements.

Strengths

The researchers can claim that this study is the first systematic review conducted to determine the Prevalence of proteinuria among Iranian children. The present study was conducted on the basis of a systematic review plan and all databases were searched. Population-based studies were also applied to the final research.

Conclusion:

While the prevalence of asymptomatic proteinuria in various studies in Iran has been widely differentiated, high levels of proteinuria were reported in Iranian children according to the findings of the present study. In order to justify and accurately diagnose the prevalence and causes of asymptomatic proteinuria as a key indication of kidney diseasein Iranian children, more detailed studies are required with a larger sample size in all provinces in Iran.

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