

Ramadan Fasting and Kidney Stones: A Systematic Review

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ABSTRACT

Purpose: Ramadan fasting in Muslims may contain several hours of abstaining from food and drinking in any kind. This can potentially increase the risk of urinary stone disease. Current literature on possible effects of Ramadan fasting on urolithiasis is rather limited. Having the gap in scientific background, we decided to evaluate the available comparative information in this systematic review.

Materials and Methods: We included all studies comparing fasting and non-fasting conditions, studies evaluating stone formation and clinical manifestations of kidney stone disease. All the English studies published from January 1980 to the end of 2019 were included. The exclusion criteria were as followed: fasting out of Ramadan, non-comparative studies, animal studies, patients with bladder stones and studies evaluating conditions that are only indirectly related to the stone formation or clinical manifestations of it. Applying the Joanna Briggs Institute (JBI) methodology for systematic review showed the quality of included studies was not high.

Results: Only five studies remained after exclusion. Meta-analysis was not applicable due to the diversity in methods and evaluated population.

Conclusion: Main trend of the included studies is toward showing no difference between fasting and non-fasting conditions in terms of renal stone formation. However, generalization of the findings to greater populations should be applied carefully considering the heterogeneity of results and quality of studies.

Keywords: Fasting; Kidney Calculi; Kidney Diseases; Systematic Review

INTRODUCTION

Ramadan is the ninth month of the Islamic lunar calendar, during which Muslims fast for a whole month. Fasting in Ramadan means abstaining from eating, drinking and smoking from dawn to dusk. Some conditions, either physiological or pathophysiological, can exempt one from fasting, including pregnancy, breastfeeding and some disabilities (at their own discretion or the doctor's) ^(1,2). Muslims eat two meals a day during this month. One meal before dawn, known as Sahar, and the other after sunset, called Iftar. ⁽³⁾ Complete restriction of food and fluids intake from sunrise to sunset in can lead to different levels of dehydration in fasting people.

Due to the low intake of fluids, the body responds to these changes by reducing urine output and increasing urine concentration as an attempt to reach normal homeostasis. ⁽⁴⁾ If proper care is not taken to ensure a hydrating diet during non-fasting hours, dehydration can be a serious complication and can even lead to death. ⁽⁵⁾

Due to the increased urine concentration resulting from low fluid intake, changes in the renal system are expected to occur in order to adapt the body to the dehydrated state. Nevertheless, some studies show that in spite of these changes, there is no deterioration in renal function in healthy individuals and even in some patients with chronic kidney disease. ⁽⁶⁾ However, there are still concerns about fluid restriction in people with chronic kidney disease. Some data, although not conclusive, suggest that fasting can alter the renal tubular system in people with chronic kidney disease. ^(7,8)

Another issue is the direct effects of Ramadan fasting on urinary stone formation. In available literature, controversial findings have been reported in this regard. Several studies have shown that fluid restriction and dehydration increase the risk of urolithiasis. ⁽⁹⁾ Most studies failed to find such relationship. ⁽¹⁰⁻¹⁴⁾

In addition, the role metabolic status has been suggested as a possible factor in evaluation of lithogenic factors. For instance, the collection of some etiologic factors of stone formation may play a pathogenic role more that it was previously assumed. ⁽¹⁵⁾

Several studies have tried to declare the effect of Ramadan fasting on urinary stone formation. However, most of them are methodologically weak with different study designs, various outcome measures and conclusions. Considering the high incidence of fasting among Muslims and the fact that the characteristics of this matter have not been dealt with in depth, we decided to run a systematic review evaluating the effect of Ramadan fasting on urolithiasis.

METHODS AND MATERIALS

This systematic review was conducted in accordance with the JBI methodology for systematic review of prevalence evidence⁽¹⁶⁾ and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)⁽¹⁷⁾ to make sure the methods and reporting of data is comprehensive and transparent.

The question of this review was as followed: "Does Ramadan fasting affect urinary stone formation or clinical manifestation in people who fast continuously during Ramadan?"

Inclusion and Exclusion Criteria

We included any study which evaluated people who fast uninterruptedly and compared them with non-fasting people or with themselves while they were not fasting. All observational studies including prospective and retrospective cohort, case-control and cross-sectional studies were included in this review. Studies published in English from 1980 till the end of 2019 were considered for inclusion in the current review.

Exclusion criteria were as follows: 1) Fasting out of Ramadan conditions, 2. Non-comparative studies (reviews, case series, reports...) 3. Animal studies, 4. Patients with bladder stones (due to different nature of pathogenesis) and 5. Studies evaluating conditions that are only indirectly related to the stone formation or clinical manifestations of it (acid-base balance, changes in specific gravity...).

Target population consists of people who fast continuously during the month of Ramadan.

Outcome measures included both clinically symptomatic presentation of stone disease (renal colic, obstructive uropathy, urinary retention...) and asymptomatic finding of evidence in favor of urolithiasis (imaging or laboratory findings).

Search Strategy

We searched PubMed, Embase, Scopus, ProQuest, Web of Science and The Cochrane Library. PubMed database was searched using the following keywords: "fasting", "ramadan fasting", "ramazan fasting", "islamic fasting", "food abstinence", "fasting in Islam", the term *ramadan* was added

to different terms used for urinary stones disease (urolithiasis/ urinary lithiasis, urine calculi/ calculus, kidney stone / stones and many other phrases offered via Mesh). For Embase a specific keyword set was used. We first included all of the studies from January 1980 until the end of 2019. We screened reference lists of included studies and review articles. The full search strategy for PubMed and Embase is provided in **Appendix I**.

Study selection

Following the search, all identified citations were imported into EndNote X9.1 and duplicates were removed.

Two independent reviewers (FS & HG) screened titles and abstracts for eligibility criteria of the review. The full text of potentially eligible studies was retrieved and assessed in detail against the inclusion criteria by the mentioned reviewers. Studies that did not meet the inclusion criteria were excluded. Any disagreements between the reviewers were resolved through discussion, or by referring to a third reviewer (MA).

Assessment of methodological quality

Two independent reviewers (FS & HS) critically appraised eligible studies at the study level using standardized critical appraisal instruments from the Joanna Briggs Institute JBI Critical Appraisal Checklist for Analytical Cross Sectional and/ or Case Control Studies. **(Figure 2, 3)** Any disagreements between the reviewers were resolved through discussion. The details of the study qualities are presented in **Table 1**.

Data extraction

Two independent reviewers extracted data from included studies using modified standardized JBI data extraction tool.⁽¹⁶⁾ The data extracted included populations, sample size, study methods, publication year, and region of study, mean age, gender, and outcome measurement. The reviewers resolved disagreements through discussion. Extracted data from included studies is presented in **Table 2**.

RESULTS

Study inclusion

Comprehensive electronic searching identified 181 studies. In the screening steps of title, abstract and full-text, two reviewers selected 106 studies, and finally 5 observational studies remained for critical appraising process. The PRISMA flowchart of this process is represented in **Figure 1**.

Meta-analysis could not be performed because of heterogeneity in terms of methods, objectives and findings. Among the included five studies, four of them evaluated the occurrence rate of renal colic in Ramadan-fasting people, although in different methods.

Characteristics of the included studies

The characteristics of the included studies are summarized in **Table 2**.

Norouzy, et al ⁽¹⁸⁾ in 2011 evaluated the number of patients admitted with renal colic during various stages of peri-Ramadan month. This was a prospective observational study. They defined four stages of two-week periods starting two weeks before Ramadan (stage 1) and finishing two weeks after Ramadan (stage 4). The authors found that the occurrences of renal colic among all 610 patients in two major hospitals were increased significantly during the first two weeks of Ramadan (stage 2). However, the number of admissions decreased during the last two weeks of Ramadan and two weeks after Ramadan (stage 3 and 4). They also noticed the mean room temperature for each group (27.7°C, 24.8°C, 23.5°C, and 21.2°C for stages 1 to 4 respectively). This is important especially when we face the results of other studies.

Al Mahayni, et al ⁽¹⁹⁾ retrospectively evaluated 237 patients admitted through the Emergency Room (ER) with a diagnosis of renal colic secondary to urinary stones over a 10-year period and compared Ramadan versus non-Ramadan months, as well as Ramadan in the summer (between 41-45 degrees Celsius) versus in the winter (21-24 degrees Celsius) among these patients. They concluded that Ramadan fasting did not increase the risk for developing urinary stones compared to non-fasting months. However, fasting in Ramadan during the summer may increase the risk of developing ureteral stones compared to fasting in winter. They also mentioned that the possibility of finding a urinary stone in ureter during Ramadan is more likely than other locations of urinary system.

Basiri, et al ⁽¹¹⁾ evaluated monthly variations of renal colic in 574 patients in a 12-month period, 43 of which presented during Ramadan. They found that high temperature rather than fasting can lead to increased colicky pain episodes. There were seven lunar months with more than 43 presented patients.

Cevik, et al ⁽²⁰⁾, evaluated 176 patients with ureteric colic (89 before Ramadan, 87 in Ramadan) also showed that fasting did not change the number of ureteric colic visits. They also showed that despite some changes in urinary metabolites by fasting, there is not enough evidence that these changes increase urinary calculus formation.

Miladpour, et al ⁽¹²⁾ evaluated biochemical laboratory findings of urine and blood samples as well as renal ultrasonography in 57 patients (37 recurrent calcium stone formers and 20 people without history of urolithiasis) in fasting and non-fasting conditions. We should be cautious about the findings since changes in many of these tests cannot necessarily result in stone formation. However, some of the parameters like ultrasonography studies were objective means, directly addressing the stone. The authors found a number of effects on total excretion and concentrations of urinary precipitate and inhibitory elements but they concluded that enough evidence in favor of increased risk of calculus formation could not be found.

DISCUSSION

The studies evaluated for this systematic review are not sufficiently informative about the effects of Ramadan fasting on urinary stone disease.

This lack of conclusiveness was the result of different factors, some of which are discussed below:

1. *Methodological diversity*: the studies were quite different in their methods. Some are retrospective and others prospective, with various focus points, which can affect the overall results.

2. *Quality:* No randomized clinical trials were available, which makes sense considering it is hardly feasible to randomize people in fasting and non-fasting groups. None of our included studies met the good quality characteristics of JBI checklist except in rare aspects (Table.1).
3. *Study objectives:* Four out of five studies used the frequency or monthly trend of acute renal colic, comparing non fasting condition with fasting as their main outcome. Although this can be one aspect of clinical manifestations, it is an oversimplification of a complex multifactorial process, considering the fact that stone formation does not necessarily result in renal colic in a given time frame. In other words, a small nidus of stone can be first formed in kidneys during the fasting period, turning to a visible, clinically important stone later, when it may not seem to be related to fasting.

One other important aspect of choosing symptomatic stone passage as a means for evaluation of stone formation is the possibility of missing "asymptomatic stone passages". D'Costa et al, ⁽²¹⁾ showed that among a group of patients with asymptomatic small kidney stones, at 5 years there was a CT scan-detected stone passage rate of 51 percent, only about half of which were accompanied by symptoms. This finding means that small stones may pass without obvious clinical symptoms and the stone formation rate can be underestimated using ureteric colic as the outcome of interest.

4. *Seasonal changes in Ramadan:* since the lunar year is ten days shorter than solar year, month of Ramadan lies in different seasons during a long time frame. When it lies in summer, especially in hot climate, longer day hours and higher temperature may be related to a higher risk of dehydration and resultant stone formation rate. This is a possibility not appropriately addressed in all of the studies included.
5. *Heterogeneous results:* Even among these rare studies, the results are not homogenous. Norouzy et al, ⁽¹⁸⁾ showed a significant difference in clinical presentation of renal colic during the first two weeks of Ramadan compared to the other stages before and after this period. This increase-decrease pattern was the same in two different hospitals evaluated in this study, showing that possibly this is not a random finding. Others however, could not find such relationship. Instead, they found that the hot climate is much more likely than Ramadan fasting itself to affect urolithiasis.
5. Ignoring other possible factors: In the meantime, the effect of combining two or more risk-producing conditions on urinary stone disease has not been properly identified in the literature. As an instance, it is not clear whether Ramadan fasting in summer and hot climate areas, would add an additional risk of stone formation to the risk attributed to the climate only? Does coincidence of polycystic kidney disease, severe hypertension, diabetic nephropathy or different levels of chronic kidney disease PLUS fasting in Ramadan, apply an additional risk of calculus formation to the kidneys?

Conclusion

The effect of combining two or more risk-producing conditions on urinary stone disease has not been properly identified in the studies. Due to the poor quality of the current literature as discussed, it is impossible to form a generalized opinion on whether fasting in Ramadan affect the stone formation. For instance, it is not clear whether Ramadan fasting in summer and hot climate areas, would add an additional risk of stone formation to the risk attributed to the climate only? Does coincidence of polycystic kidney disease, severe hypertension, diabetic nephropathy or different levels of chronic kidney disease in addition to fasting in Ramadan, apply an additional risk of calculus formation to the kidneys? This issues can be addresses in future studies.

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Appendix: <https://journals.sbmu.ac.ir/urolj/index.php/uj/libraryFiles/downloadPublic/10>

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3	Basiri, et al (2004)	☹️	☹️	😊	😊	😊	😊	😊	😊	-	-
4	Cevik, et al (2016)	😊	😊	😊	😊	😊	😊	😊	😊	-	-
5	Miladipour, et al (2012)	😊	😊	😊	😊	😊	😊	😊	😊	😊	☹️

😊: Low risk ☹️: High risk 😊: Unclear risk

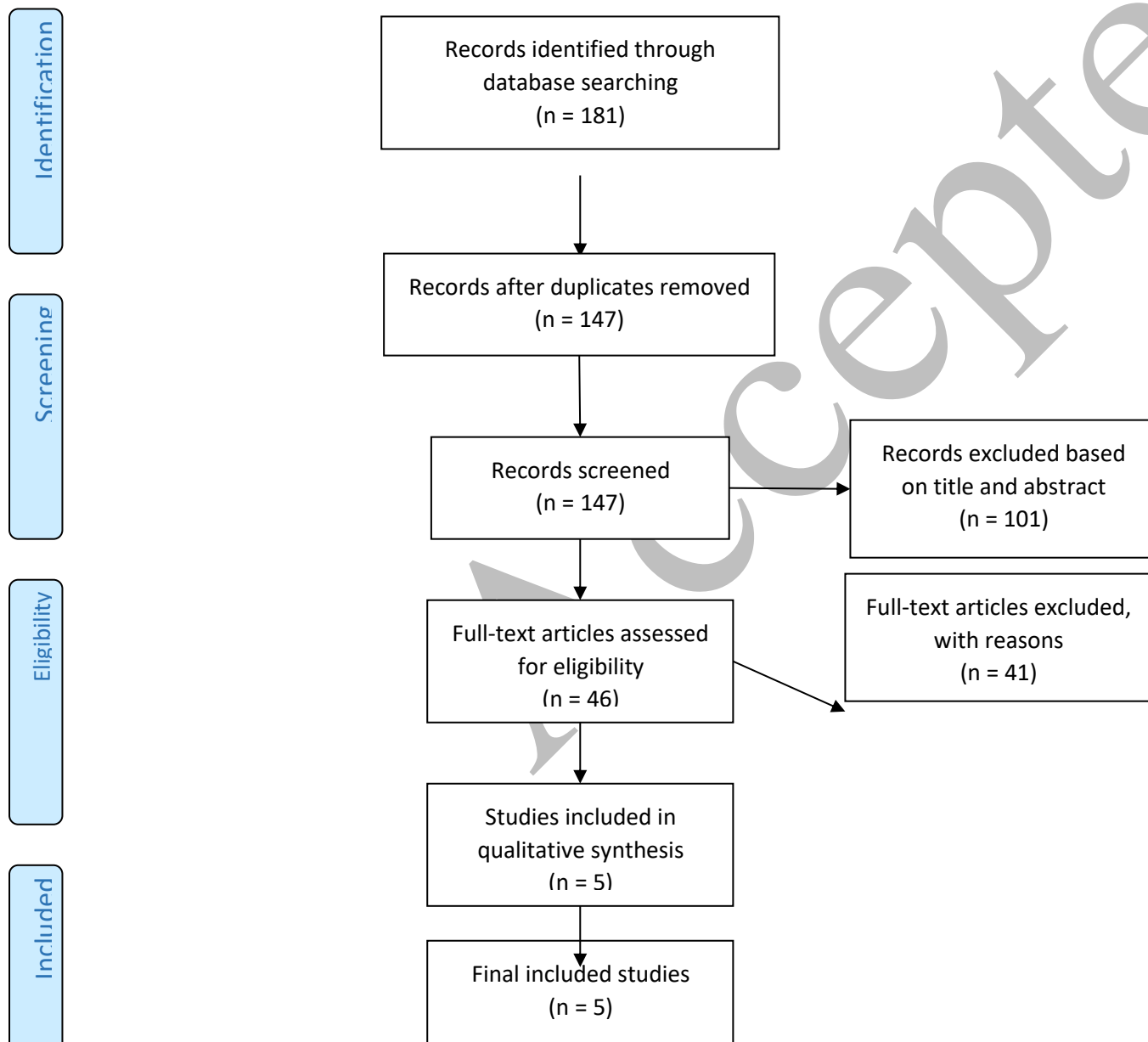
*Description of questions in JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies and Case-Control are listed in Figures 2 and 3.

Table 2. Characteristics of included studies.

No.	Author	Year	Study design	Country	Population	Sample size	Subject characteristics			Study duration (months)	Methods for Outcome measurement	Results
							Male	Females	Age (mean)			
1	Norouzy A, et al, 2011	2011	Prospective observational study	Mashad/Iran	Renal colic due to	610	441	169	37.6 (range)	2 weeks prior Ramadan	Symptoms of renal colic based on	A significant increase in the incidence of ureteric colic during Ramadan.

					urinary tract stones.				15-85 years)	till 2 weeks after Ramadan	physician's clinical judgment.	
2	Al Mahayni A, et al, 2018	2018	Retrospective	Riyadh/ Kingdom of Saudi Arabia	Renal colic due to urinary tract stones.	237	178	59	45.8	1	Confirmed clinically and radiologically (non-contrast CT scan)	Fasting in Ramadan does not increase the risk for developing urinary stones compared to non-fasting months. Ramadan in summer may increase the risk of developing ureter stones compared to fasting in Ramadan during the winter.
3	Basiri, et al, 2004	2004	Retrospective	Varamin/Iran	Renal Colic due to urinary tract stones.	574	398	176	36.4	1	Acute attack of renal colic	Higher temperature rather than fasting is a cause for ureteric colic.
4	Cevik Y, et al, 2016	2016	Prospective observational study	Turkey	Renal Colic due to urinary tract stones.	176	112	64	40.47 (range 18-81 years)	2	Physician's clinical judgment according to classical clinical features, history, and physical examination. CT in no definite diagnoses.	No change in visits related to renal colic during Ramadan.
5	Miladipour A, et al, 2012	2012	Case-Control	Tehran/Iran	37 recurrent calcium calculus formers and 20 with no history of kidney calculi	57	57	-	41.66	1	Urine metabolite concentrations and supersaturations during fasting and non-fasting periods in recurrent calcium calculus formers and healthy controls	Fasting during Ramadan had different effects on total excretion and concentrations of urinary precipitate and inhibitory factors contributing to calculus formation.

Figure 1. PRISMA flow diagram of selection process



JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the study subjects and the setting described in detail?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the exposure measured in a valid and reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were objective, standard criteria used for measurement of the condition?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were confounding factors identified?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were strategies to deal with confounding factors stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes measured in a valid and reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Comments (Including reason for exclusion)

Figure 2. JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies.

Accepted

JBI Critical Appraisal Checklist for Case Control Studies

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not applicable
1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were cases and controls matched appropriately?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Were the same criteria used for identification of cases and controls?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Was exposure measured in a standard, valid and reliable way?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Was exposure measured in the same way for cases and controls?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were confounding factors identified?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were strategies to deal with confounding factors stated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was the exposure period of interest long enough to be meaningful?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Was appropriate statistical analysis used?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Comments (Including reason for exclusion)

Figure 3. JBI Critical Appraisal Checklist for Case-Control studies.

Accepted