



# The correlation between low-dose aspirin consumption in pregnancy and fetal kidney size: a prospective case-control study

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## ABSTRACT

**Introduction:** Low-dose aspirin (LDA) has been widely studied for its benefits in preventing preeclampsia and other pregnancy complications.

**Objectives:** Research indicates that aspirin may improve placental vascularization and fetal growth outcomes, particularly in high-risk populations. However, the specific impact of aspirin on fetal organ development, such as kidney size, remains underexplored.

**Patients and Methods:** This prospective case-control study was conducted to assess the correlation between LDA consumption and fetal kidney size among pregnant women referred to Imam Khomeini hospital in 2024. Participants were divided into two groups those consuming LDA and those who did not. A structured questionnaire was used to collect demographic and medical history data, including details on aspirin use. Fetal kidney size was evaluated using standardized color Doppler ultrasound techniques. Data were compared between two groups of case and control using statistical tests, specifically linear regression.

**Results:** The study included 144 mothers, evenly divided into two groups; a control group and a case group, each consisting of 72 participants. Maternal and gestational characteristics were similar between the two groups. The analysis revealed significant negative correlations between the intake of LDA and fetal kidney size, indicating that increased aspirin consumption was associated with reductions in both the lengths and widths of the right and left kidneys.

**Conclusion:** The findings of this study indicated a concerning association between LDA consumption during pregnancy and reduced fetal kidney size, suggesting that increased aspirin intake may adversely affect renal development in the fetus.

### Implication for health policy/practice/research/medical education:

In a prospective case-control study on 144 mothers, we found a concerning association between low-dose aspirin (LDA) consumption during pregnancy and reduced fetal kidney size, suggesting that increased aspirin intake may adversely affect renal development in the fetus.

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## Introduction

Pregnancy is a physiological process that typically lasts about 40 weeks and is divided into three trimesters (1). During the first trimester, significant changes occur in a woman's body, including the implantation of the fertilized egg and the development of the placenta, which provides nutrients to the embryo (2). The second trimester is often referred to as the golden period of pregnancy because many women experience fetal growth accelerates and at the end of this trimester, many women can feel fetal movements (3). In the third trimester, the fetus continues to grow and prepare for birth, leading to physical discomfort for the mother due to the increased size of the fetus (4). Regular prenatal care is essential for monitoring both maternal and fetal health, as pregnancy can come with risks such as gestational diabetes, preeclampsia, and preterm labor (5). Aspirin is a widely used medication that can have significant implications during pregnancy. Low-dose aspirin (LDA) is often recommended for certain pregnant women to reduce the risk of complications such as preeclampsia, especially in those with a history of this condition or other risk factors (6). The administration of LDA has been shown to improve outcomes for both mothers and infants by decreasing the incidence of preterm birth and low birth weight (7). However, the timing of aspirin administration is crucial; since, it is generally advised to start LDA therapy between 12 and 16 weeks of gestation for optimal benefits (8). While LDA is considered safe for most pregnant women, high-dose aspirin should be avoided due to potential risks, including bleeding complications during delivery (9). Pregnant women should always consult their healthcare provider before starting or continuing any medication, including aspirin, to ensure it is appropriate for their specific health circumstances (10). Research continues to explore the long-term effects of prenatal aspirin exposure on child development, but current evidence suggests that low-dose use does not pose significant risks to the fetus (11). Low-dose aspirin is often prescribed to pregnant women at risk for conditions such as preeclampsia, which can adversely affect kidney health (12). Some studies suggest that LDA may help improve renal perfusion and function in pregnant women, particularly those with hypertension (13). However, high doses of aspirin are associated with an increased risk of renal complications, including acute kidney injury, especially in the context of dehydration or other risk factors (14). Furthermore, fetal exposure to high doses of aspirin has raised concerns about potential adverse effects on renal development and function in newborns (15). Therefore, LDA can be beneficial in certain cases; however, careful consideration and monitoring are essential to mitigate any risks to maternal and fetal kidney health (16). Consequently, this study was conducted to determine whether LDA can influence renal development in the fetus, particularly in pregnant women at risk for complications such as preeclampsia who need

this medication. Additionally, this study seeks to evaluate any potential adverse effects associated with LDA on fetal kidney health, thereby contributing to the understanding of its safety and efficacy in clinical practice.

## Objectives

The objective of this study is to investigate the correlation between LDA consumption during pregnancy and fetal kidney size among pregnant women referred to Imam Khomeini hospital in 2024. By employing a prospective case-control design, the study aims to determine whether LDA intake is associated with significant changes in the dimensions of fetal kidneys, thereby contributing to the understanding of the implications of aspirin use on fetal organ development. The findings are expected to provide valuable insights for prenatal care practices, particularly regarding the risks and benefits of LDA in managing pregnancy complications.

## Materials and Methods

### Study design and participants

This prospective case-control study was designed to assess the relationship between LDA consumption and fetal kidney size among pregnant women. Participants were recruited from Imam Khomeini hospital in 2024, and they were categorized into two groups cases (those consuming LDA and control (those who do not use LDA).

### Inclusion and exclusion criteria

The study included pregnant women aged 18-45 years, who have provided informed consent to participate in the study, with gestational ages ranging from 26 to 30 weeks at recruitment. Exclusion criteria included significant maternal comorbidities and contraindications to aspirin consumption.

### Participant selection and sampling

Participants were selected from the obstetrics and gynecology department of Imam Khomeini hospital. Pregnant women (n = 72) who report regular consumption of LDA (defined as 80 or 160 mg daily) for at least four weeks before recruitment were categorized into the case group. The control group (n = 72) consisted of pregnant women who did not consume LDA. Participants in this group were matched to those in the case group based on maternal age, gestational age, and other relevant demographic factors. All participants were in the gestational age of 26 to 30 weeks.

### Data collection

At the beginning of this study, written informed consent was obtained from all participants to ensure ethical compliance and participant autonomy. A structured questionnaire was administered through interviews, capturing essential demographic and medical history information, including the mother's age, past-medical

history (PMH), body mass index (BMI), gestational age, number of pregnancies, live births, and abortions, as well as details regarding amniotic fluid index (AFI) and aspirin usage. For participants in the case group, specific details about their aspirin use, including dosage and duration, were meticulously recorded. Fetal kidney size was assessed using standardized color Doppler ultrasound techniques during the gestational period of 26 to 30 weeks. Measurements included the anteroposterior and lateral diameters of the kidneys, which were documented for subsequent analysis.

### Outcomes

The outcomes of this study focused on elucidating the correlation between LDA consumption during pregnancy and fetal kidney size, specifically measuring kidney length and width.

### Statistical analysis

Data were analyzed using the Statistical Package for Social Science (SPSS) version 27 (IBM Corp, USA), employing various statistical methods to evaluate the relationships between LDA consumption and fetal kidney size. Chi-square test was utilized to assess associations between categorical variables and the independent T-tests were conducted to compare the quantitative variables across the two groups of case (LDA users) and control (non-users). Furthermore, both univariate and multivariate linear regression analysis were performed to investigate the correlation between kidney size and LDA consumption status, allowing for the adjustment of potential confounding factors. A *P* value of less than 0.05 was established as the threshold for statistical significance.

### Results

The study encompassed 144 mothers, evenly divided into two groups; a control group of 72 mothers who did not consume aspirin and a case group of 72 mothers who used aspirin, with 29 taking a dosage of 80 mg and 43 taking 160 mg. The mean duration for the initiation of LDA consumption among the case groups was observed to be  $14.61 \pm 2.72$  weeks. A significant majority reported no PMH, while a smaller proportion indicated a history of such conditions. The average age of the mothers was slightly above 30 years, and the mean fetal age was in the third trimester of pregnancy. The mothers' average BMI categorized them as overweight. Furthermore, the data revealed that the mean number of pregnancies and live births suggested a trend toward multiparity, with a relatively low average number of abortions reported. Lastly, the AFI readings indicated a generally healthy range among the participants, reflecting favorable conditions for fetal development. The average length of the right kidney is slightly greater than that of the left kidney, while the average width of both kidneys is comparable, with the right kidney being marginally wider (Table 1).

The comparison between the case group of aspirin consumers and the control group revealed various health-related variables. In terms of PMH, a majority of participants in both groups reported no prior medical issues and the difference between the two groups was statistically non-significant. When examining maternal characteristics, the average age of mothers in the case group was slightly higher than that of the control group; the gestational age of fetuses showed a minimal difference between the two groups; and maternal BMI was higher in the control group; however, no statistically significant

**Table 1.** Demographic characteristics and sonographic findings of the included mothers in the study

Variable	Sub-variable	Frequency	Percent		
Past-medical history	No	114	79.2		
	Yes	30	20.8		
Aspirin consumption (mg)	No	72	50		
	80	29	20.1		
	160	43	29.9		
Variable	Mean	SD	Min	Max	
Mother's age (y)	30.59	6.15	18	45	
Fetal's age (wk)	27.54	1.45	26	30	
Mothers's BMI (kg/m <sup>2</sup> )	27.84	4.62	17.67	39.26	
Gravida (N)	2.24	1.35	1	7	
Para (N)	0.88	1.05	0	5	
Abortus (N)	0.36	0.74	0	4	
AFI (cm)	12.26	2.52	7.47	22	
LDA consumption initiation in case group (from week)	14.61	2.72	13	22	
Right kidney length size (mm)	28.71	3.172	20.20	37.10	
Right kidney width size (mm)	16.39	2.44	11.00	28.00	
Left kidney length size (mm)	28.57	3.21	21.00	37.00	
Left kidney width size (mm)	16.21	2.62	9.00	30.00	

SD, Standard deviation; Min, Maximum; Max, Maximum; BMI, Body mass index; AFI, Amniotic fluid index; N, Number; LDA, Low-dose aspirin.

different was found between two groups regarding three variables. Other variables such as gravida, para, abortus, and AFI also did not show notable differences between the groups. However, statistically significant disparities were observed in kidney measurements; both the right and left kidney lengths and widths were larger in the case group compared to the control group (Table 2).

Table 3 highlights the correlation between kidney size and aspirin consumption through univariate linear regression in unadjusted conditions of variables. The analysis indicated that for every unit increase in LDA consumption, the right kidney length decreases by approximately 1.69 mm. Similarly, the right kidney width is associated with a decrease of about 1.33 mm. The left kidney length showed a more pronounced reduction of approximately 2.14 mm per unit increase in LDA consumption and the left kidney width decreased by around 1.35 mm. All associations are statistically significant, with *P* values indicating strong correlations for both kidney lengths and width size with aspirin use (Table 3).

After adjusting variables for confounders, including

maternal age, previous medical history, BMI, fetal age, number of pregnancies, live births, abortions, and amniotic fluid index (AFI), the results demonstrated a significant correlation for right kidney length, with an unstandardized coefficient (B) of -1.75, and a 95% confidence interval (CI) ranging from -2.71 to -0.78. This suggests that for each unit increase in LDA consumption, the right kidney length decreases by approximately 1.75 mm. Similarly, the right kidney width showed a B of -1.25 and a CI from -2.04 to -0.47. The left kidney length also demonstrated a significant relationship with aspirin consumption, evidenced by a B of -1.99, and a 95% CI between -2.95 and -1.03. Lastly, the left kidney width was found with a B of -1.23 and a CI ranging from -2.05 to -0.41. These results suggest that aspirin consumption is associated with reduced kidney size across various measurements (Table 4).

### Discussion

The results of our study demonstrated a significant inverse relationship between maternal aspirin consumption and

**Table 2.** Frequency distribution of demographic characteristics and sonographic findings of participants between two groups of case (aspirin consumer) and control (no consumption aspirin)

Variable	Aspirin consumption				P value	
	Control group (n = 72)		Case group (n = 72)			
	N	%	N	%		
Past medical history	No (n = 114)	56	49.1	58	50.9	0.682*
	Yes (n = 30)	16	53.3	17	46.7	
Variable	Mean	SD	Mean	SD	P value	
Mother's age (y)	29.73	6.39	31.44	5.82	0.096**	
Age of infants (wk)	27.62	1.32	27.47	1.57	0.530**	
BMI of mothers (kg/m <sup>2</sup> )	27.27	4.86	28.40	4.32	0.143**	
Gravida (N)	2.13	1.26	2.36	1.43	0.297**	
Para (N)	0.80	1.03	0.92	1.08	0.694**	
Abortus (N)	0.28	0.53	0.44	0.90	0.180**	
AFI (cm)	12.09	2.78	12.43	2.23	0.410**	
Right kidney length size (mm)	29.56	3.15	27.86	2.97	0.001**	
Right kidney width size (mm)	17.06	2.41	15.73	2.30	<0.001**	
Left kidney length size (mm)	29.64	3.20	27.49	2.86	<0.001**	
Left kidney width size (mm)	16.89	2.78	15.53	2.82	0.002**	

SD, Standard deviation; Min, Maximum; Max, Maximum; BMI, Body mass index; AFI, Amniotic fluid index; N, Number; LDA, Low-dose aspirin.

\* Chi-square; \*\* Independent T-test.

**Table 3.** The correlation between kidney size and aspirin consumption using univariate linear regression (unadjusted)

Kidney size	Aspirin consumption			
	P value	B	95% CI	
			Lower	Upper
Right kidney length size (mm)	0.001	- 1.69	-2.70	-0.68
Right kidney width size (mm)	<0.001	-1.33	-2.11	-0.55
Left kidney length size (mm)	<0.001	-2.14	-3.14	-1.14
Left kidney width size (mm)	0.002	-1.35	-2.19	-0.51

CI, Confidence interval; B; Unstandardized coefficient.

**Table 4.** The impact of aspirin consumption on kidney size using multivariate linear regression (adjusted)

Kidney size	Aspirin consumption			
	P value	B	95% CI	
			Lower	Upper
Right kidney length size (mm)	<0.001	-1.75	-2.71	-0.78
Right kidney width size (mm)	0.002	-1.25	-2.04	-0.47
Left kidney length size (mm)	<0.001	-1.99	-2.95	-1.03
Left kidney width size (mm)	0.003	-1.23	-2.05	-0.41

CI, Confidence interval; B; Unstandardized coefficient.

fetal kidney size, indicating that increased use of aspirin correlates with a reduction in both the length and width of the kidneys. This finding suggests that aspirin may have a detrimental effect on renal dimensions, potentially implicating its role in renal health deterioration. Specifically, our analysis revealed that individuals who regularly consume aspirin exhibited a measurable decrease in kidney size compared to non-users, raising concerns regarding aspirin therapy's long-term implications on renal morphology and function.

This study represents a pioneering investigation into the impact of aspirin consumption during pregnancy on fetal kidney size, addressing a significant gap in the existing literature. Prior research has extensively explored various aspects of maternal medication use and its implications for fetal development; however, the specific influence of aspirin on renal morphology has not been previously examined. By focusing on this under-researched area, the study aims to provide valuable insights into potential developmental outcomes associated with aspirin intake during gestation, thereby contributing to a more comprehensive understanding of prenatal factors that may affect fetal organ development. The findings could have important implications for clinical guidelines regarding medication use in pregnant populations, highlighting the need for further research to elucidate the mechanisms underlying any observed effects on fetal kidney size.

Zhang et al found that concerns have been raised regarding the potential negative effects of high-dose aspirin exposure during fetal development, particularly on renal development and function in newborns (15). On the other hand, in contrast to our findings, which suggest that LDA use may lead to decreased kidney function as a result of its adverse effects on kidney size, another study has reported that LDA can improve renal blood flow and overall kidney function in pregnant women, particularly those with hypertension (13).

Previous studies have explored the effects of various substances on fetal kidney development, with some research indicating that maternal factors such as diet and body composition can influence renal growth. For instance, a study focusing on Indigenous Australian women found that while maternal nutrition impacted fetal growth, it did not significantly affect fetal kidney volume

(17). This suggests that while maternal dietary intake is crucial for overall fetal health, other factors, including medication use like aspirin, may play a more direct role in renal development.

Additionally, another study examining the impact of maternal obesity on fetal kidney development indicated that increased body fat negatively affected renal structure in offspring (18). This aligns with our findings, as both aspirin consumption and maternal obesity could represent modifiable risk factors influencing kidney morphology. However, unlike obesity, which has been shown to have a clear negative impact on kidney function and development, the specific mechanisms by which aspirin affects fetal kidneys remain less understood.

The implications of these findings are critical for clinical practice. Given that aspirin is commonly prescribed for various conditions during pregnancy, understanding its potential effects on fetal kidney development is essential. The reduction in kidney size observed in our study could imply long-term consequences for renal function in offspring, necessitating further research into the safety of aspirin use during pregnancy. Overall, our study highlights a significant inverse relationship between maternal aspirin consumption and fetal kidney size, suggesting potential adverse effects on renal development. While previous research has established links between maternal factors and fetal health, our findings specifically underscore the need to consider medication use as a critical factor influencing renal morphology. Future investigations should focus on elucidating the mechanisms underlying the impact of aspirin on fetal kidney development and assessing the long-term implications for renal health in children exposed to aspirin in utero. Given the widespread use of aspirin among pregnant women, these insights are vital for guiding clinical recommendations and ensuring optimal fetal health outcomes.

## Conclusion

The results of this study indicate a significant negative correlation between LDA consumption and fetal kidney size, with findings revealing that increased aspirin intake is associated with reductions in both kidney length and width. Specifically, the analysis demonstrated that for every unit increase in LDA consumption, the right kidney

length decreased by approximately 1.75 mm, while the right kidney width decreased by 1.25 mm. Similarly, the left kidney length showed a notable decrease of 1.99 mm, and the left kidney width was reduced by 1.23 mm with increased aspirin use. These results suggest that LDA consumption during pregnancy may adversely affect fetal kidney development, highlighting the need for careful consideration of aspirin use in prenatal care to mitigate potential risks to fetal organ growth. Given these results, healthcare providers should consider the potential implications of aspirin use during pregnancy and weigh the benefits against the possible negative effects on fetal health, particularly regarding kidney development. Further research is warranted to explore the underlying mechanisms and to establish guidelines for safe aspirin use in pregnant populations.

### Limitations of the study

First, the reliance on self-reported data regarding LDA consumption may introduce recall bias, as participants might not accurately remember or disclose their usage patterns. Secondly, the study's sample size, while adequate for preliminary findings, may limit the generalizability of the results to broader populations, particularly in diverse demographic settings. Additionally, potential confounding factors such as other medications, lifestyle choices, and underlying health conditions were not fully controlled for, which could influence fetal kidney development and skew the observed correlations. Lastly, the cross-sectional nature of the data collection restricts the ability to establish causality between LDA use and changes in fetal kidney size.

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### Authors' contribution

**Conceptualization:** Maryam Aliasgharpoor and Fahimeh Ghotbizadeh.

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**Resources:** All authors.

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**Writing—original draft:** All authors.

**Writing—reviewing and editing:** All authors.

### Conflicts of interest

The authors declare no conflict of interest.

### Ethical issues

The research was conducted in accordance with the Declaration of Helsinki. This study resulted from the research project (No. 71459), with the ethical code # IR.TUMS.IKHC.REC.1403.286 (<https://ethics.research.ac.ir/EthicsProposalView.php?id=504356>), approved by the Tehran University of Medical Sciences, Tehran, Iran. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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