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Research Article

Hypertensive and Metabolic Issues in Nephrolithiasis with Pregnancy

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2. Keywords

Nephrolithiasis; DM; hypertension

1. Abstract

1.1 Background

Renal stones are correlated clinically with forthcoming development of hypertension, diabetes, and the metabolic syndrome.

1.2 Objective of the study

To evaluate and investigate whether stone formation before pregnancy is correlated with metabolic and hypertensive medical development emergence in gestation. the research team hypothesis was based on that stone development is considered a potential marker of metabolic disease and will be linked with greater risk for maternal complications in pregnancy.

1.3 Methodology

We conducted a two-group cohort study of women who delivered infants at El Sahel teaching Hospital 2015to 20118. Women with abdominal imaging investigate (computed tomography or sonography) before pregnancy were incorporated in the analysis.923 cases were assessed for eligibility for the study 817 cases were eligible consequently they were categorized into stone formers(126 cases) and non-stone formers(691 cases .finally 110 cases were enrolled for each arm of the study 8 cases were lost during follow up in the stone former research group and 6 cases were lost during follow up in non-stone former research group. Gestational outcomes in women with documented renal stones by imaging were compared with those of women without stones on imaging. Females with preexisting chronic kidney disease, hypertension, and diabetes were excluded.

1.4 Results

Stone former research group had statistically significantly more frequent hypertension, gestational hypertension, preeclampsia and preterm(p values=0.005,0.035,0.034,0.017,consecutively) as well as higher Maximum systolic blood pressure, diastolic blood pressure and glucose tolerance test (p values<0.001,0.030,0.039,consecutively).

1.5 Conclusions

In women without preexisting diabetes, hypertension, and CKD, a history of nephrolithiasis was associated with gestational diabetes and hypertensive disorders of pregnancy, especially in women with high first trimester body mass index.

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3. Introduction

Renal stones are frequently encountered in clinical scenarios presented in every day practice, and the incidence of renal stone disease is rising, particularly in younger age groups. Even though risk issues, e.g. diet, hydration, and urine composition, are correlated with risk of stone pathological development, epidemiologic research studies have correlated nephrolithiasis with medical systemic illnesses, e.g. metabolic syndrome and cardiovascular disorders. A past medical history of nephrolithiasis raises the clinical risk of hypertensive disease and diabetes mellitus [1,2]

There are gender specific dissimilarities and variabilities in both risk factors and medical sequalae of nephrolithiasis disease. Even though nephrolithiasis is more frequent in males, the incidence of stone disease in young age groups (below 30 years old) is greater in females. Women who clinically present with symptomatic nephrolithiasis during gestation are more expected to have obstetric complications, such as premature delivery. Even though the incident rate of stone disease during gestation is not raised compared with the non-pregnant population, rising parity is correlated with greater stone development risk [3,4].

Pregnancy is an exceptional window to investigate both metabolic and cardiovascular risky issues in women. During pregnancy, there are considerable alterations in maternal metabolic pathways and systemic hemodynamics that are crucial for fetal course of development. These alterations could uncover subclinical illnesses in affected females. Transient gestational disorders, e.g. gestational DM and gestational hypertension give a predictability clinical tool for the later pathological development of DM, hypertension, and cardiovascular disease [5,6].

3.1 Aim of the Study

The aim of our research study was to observe if a history of renal stone disease raises the risk of metabolic and hypertensive complications within pregnancy in females without preexisting chronic disease.

4. Methodology

We performed a two group a cohort study of all pregnancies from El Sahel hospital medical records between January 1, 2015and December 31, 2018. Clinical information, involving medical history, prenatal BP values, and delivery information, was obtained from the medical records prospectively by research team of investigators and directly transferred into the research study database. Singleton gestations that continued beyond 20- gestational weeks were incorporated within the analysis.

Women missing baseline BP, urine dipstick, weight, or glucose testing (all standard of care) were excluded. Women with preexisting hypertension, were clinically defined as a BP before 20-gestational weeks above 140/90 mm Hg or the usage of antihypertensive medications before the beginning of pregnancy, were excluded from the research study.

Women with preexisting diabetes, defined on the basis of documentation in the obstetric medical record at the initial prenatal visit or the usage of oral hypoglycemic agents or insulin before gestation, were excluded from the research study. Females having preexisting kidney disease, involving structural kidney disease, glomerulonephritis, or estimated GFR<90 ml/min / 1.73m^{2}before pregnancy, who were observed during data review (involving review of nephrology documentation, imaging investigations, laboratory findings, and renal biopsy results) were excluded from the study. Detailed past medical history data, involving previous medical imaging, laboratory results, inpatient and outpatient medical documents were obtained. Examinations data were retrieved as part of medical care, involving inpatient hospital admissions, or emergency room visits. Radiology reports were implemented to identify stone formers and involved the site and number of renal stones.

Gestational diabetes was defined as a 1-hour glucose load test value of .140 mg/dl and two abnormal values on a 3-hour 100-g glucose tolerance test Preeclampsia was defined on the basis of BP and proteinuria measurements using urine dipstick analysis measurements made at antenatal visits. Gestational hypertension was defined as BP above 140/90 mm Hg after 20 gestational weeks (20). Preeclampsia was clinically defined as the existence of gestational hypertension and 2+ or greater proteinuria after 20 gestational weeks .Small for gestational age and large for gestation age have been clinically defined as birth weight less than the 10thcentile or greater than the 90th centile, consecutively .The composite fetal outcome was defined by premature delivery (before 37 gestational weeks), neonatal intensive care unit admission, or small for gestational age offspring.

4.1 Statistical methods

The collected research data were coded, tabulated, and statistically analyzed by usage of IBM SPSS statistics (Statistical Package for Social Sciences) software version 18.0, IBM Corp., Chicago, USA, 2009.

Descriptive statistics were conducted for quantitative research data as minimum& maximum of the range as well as mean±SD (standard deviation) for quantitative data, while it was done for qualitative research data as number and percentage.

Inferential statistical analyses were performed for quantitative variables by usage independent t-test in cases. In qualitative re-

search data, inferential statistical analyses for independent research variables were performed by usage Chi square test for differences between proportions and Fisher's Exact test for variables with small expected numbers. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant.

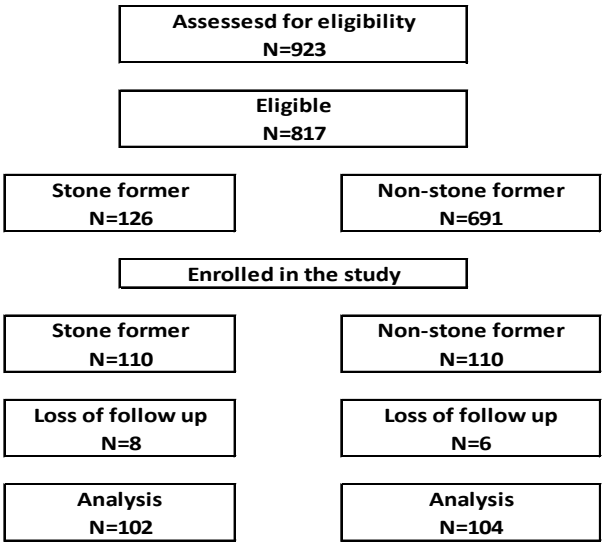

Figure 1: Flow chart of the study design

5. Results

(Figure1) 923 cases were assessed for eligibility for the study 817 cases were eligible consequently they were categorized into stone formers(126 cases) and non-stone formers(691 cases .finally 110 cases were enrolled for each arm of the study 8 cases were lost during follow up in the stone former research group and 6 cases were lost during follow up in non-stone former research group.

Among the 102 stone former, amongst had 18 (17.6%) bilateral stones, 20 (19.6%) had multiple stones& 4 (3.9%) had hydronephrosis (**Table 1**).

^Independent t-test, #Chi square test, §Fisher's Exact, *Significant, RR: Relative rate, CI: Confidence interval

Stone former research group had statistically significantly more frequent HTN,GHTN, PE and preterm(p values=0.005,0.035,0.034,0.017,consecutively) as well as higher Maximum SBP, DBP and GLT(p values<0.001,0.030,0.039,consecutively) but statistically significantly had lower GA at delivery, weight gain and birth weight(p value=0.002,<0.001,0.001,consecutively). CS and GDM were non- statistically significantly more frequent among stone former (**Table 2**).

^Independent t-test, #Chi square test, §Fisher's Exact, *Significant, RR: Relative rate, CI: Confidence interval

Bilateral stone former group significantly had more frequent HTN, PE, preterm, NICU admission and composite neonatal morbidities(p values =0.009,0.001,0.006,<0.001,0.005,consecutively) as well as higher Maximum SBP, DBP and GLT(p values= 0.002,0.001,0.041,consecutively) but significantly had lower GA at delivery, weight gain and birth weight(p values<0.001,0.001,< 0.001,consecutively). CS and GDM were non-significantly more frequent among bilateral stone former.

Table 1: Comparison between stone former and non-stone former

Variables		Stone (N=102)	Non-stone (N=104)	P	RR (95% CI)
Age (years), Mean±SD		27.9±4.1	28.3±3.9	^0.425	--
BMI (kg/m^2), Mean±SD		26.7±1.9	26.4±1.9	^0.217	--
Parity (n, %)	Primiparous	38 (37.3%)	33 (31.7%)	#0.404	--
	Multiparous	64 (62.7%)	71 (68.3%)		
Creatinine (mg/dL), Mean±SD		0.70±0.16	0.68±0.15	^0.291	--
Basal SBP (mmHg), Mean±SD		112.6±3.6	112.3±3.5	^0.520	--
Basal DBP (mmHg), Mean±SD		72.3±3.3	72.0±3.0	^0.474	--
Max SBP (mmHg), Mean±SD		135.9±10.6	127.2±9.3	**^<0.001***	--
Max DBP (mmHg), Mean±SD		80.5±15.4	76.3±12.3	**^0.030***	--
HTN, (n, %)		40 (39.2%)	22 (21.2%)	**#0.005***	1.85 (1.19–2.89)
GHTN, (n, %)		28 (27.5%)	16 (15.4%)	**#0.035***	1.78 (1.03–3.09)
PE, (n, %)		15 (14.7%)	6 (5.8%)	**#0.034***	2.55 (1.03–6.31)
CS, (n, %)		35 (34.3%)	24 (23.1%)	#0.074	1.49 (0.96–2.31)
Basal GLT (mg/dL), Mean±SD		106.2±2.8	106.4±2.8	^0.630	--
Max GLT (mg/dL), Mean±SD		112.4±13.9	109.0±9.1	**^0.039***	--
GDM, (n, %)		14 (13.7%)	5 (4.8%)	**#0.027***	2.85 (1.07–7.64)
Weight gain (kg), Mean±SD		10.7±2.8	14.6±3.5	**^<0.001***	--
GA at delivery (GA), Mean±SD		38.9±1.7	39.6±1.3	**^0.002***	--
Preterm, (n, %)		12 (11.8%)	3 (2.9%)	**#0.017***	4.08 (1.19–14.03)
Birth weight (kg), Mean±SD		3.0±0.3	3.2±0.3	**^0.001***	--
SGA, (n, %)		8 (7.8%)	3 (2.9%)	#0.113	2.72 (0.74–9.96)
LGA, (n, %)		2 (2.0%)	3 (2.9%)	§1.000	0.68 (0.12–3.98)
NICU, (n, %)		9 (8.8%)	3 (2.9%)	#0.069	3.06 (0.85–10.98)
Composite, (n, %)		15 (14.7%)	8 (7.7%)	#0.110	1.91 (0.85–4.31)

Table 2: Comparison between bilateral and unilateral stone formers

Variables		Bilateral (N=18)	Unilateral (N=84)	P	RR (95% CI)
Age (years), Mean±SD		27.2±4.2	28.0±4.1	^0.432	--
BMI (kg/m²), Mean±SD		27.2±1.6	26.6±1.9	^0.223	--
Parity (n, %)	Primiparous	9 (50.0%)	29 (34.5%)	#0.218	--
	Multiparous	9 (50.0%)	55 (65.5%)		
Creatinine (mg/dL), Mean±SD		0.69±0.10	0.70±0.17	^0.777	--
Basal SBP (mmHg), Mean±SD		112.2±4.0	112.7±3.5	^0.621	--
Basal DBP (mmHg), Mean±SD		71.9±3.4	72.3±3.2	^0.637	--
Max SBP (mmHg), Mean±SD		142.9±11.1	134.4±9.9	**^0.002***	--
Max DBP (mmHg), Mean±SD		91.5±16.2	78.2±14.2	**^0.001***	--
HTN, (n, %)		12 (66.7%)	28 (33.3%)	**#0.009***	2.00 (1.28–3.12)
GHTN, (n, %)		6 (33.3%)	22 (26.2%)	§0.567	1.27 (0.60–2.68)
PE, (n, %)		8 (44.4%)	7 (8.3%)	**§0.001***	5.33 (2.22–12.82)
CS, (n, %)		8 (44.4%)	27 (32.1%)	#0.318	1.38 (0.76–2.53)
Basal GLT (mg/dL), Mean±SD		106.6±2.8	106.2±2.8	^0.541	--
Max GLT (mg/dL), Mean±SD		118.5±17.0	111.1±12.9	**^0.041***	--
GDM, (n, %)		5 (27.8%)	9 (10.7%)	§0.069	2.59 (0.99–6.82)
Weight gain (kg), Mean±SD		8.7±3.2	11.1±2.5	**^0.001***	--
GA at delivery (GA), Mean±SD		37.1±1.6	39.3±1.4	**^<0.001***	--
Preterm, (n, %)		6 (33.3%)	6 (7.1%)	**§0.006***	4.67 (1.70–12.82)
Birth weight (kg), Mean±SD		2.7±0.3	3.1±0.3	**^<0.001***	--
SGA, (n, %)		4 (22.2%)	4 (4.8%)	**§0.031***	4.67 (1.29–16.94)
LGA, (n, %)		0 (0.0%)	2 (2.4%)	§1.000	--
NICU, (n, %)		6 (33.3%)	3 (3.6%)	**§<0.001***	9.33 (2.57–33.87)
Composite, (n, %)		7 (38.9%)	8 (9.5%)	**§0.005***	4.08 (1.70–9.82)

6. Discussion

In the current research study performed in ElSahel Teaching hospital 923 cases were assessed for eligibility for the study 817 cases were eligible consequently they were categorized into stone formers(126 cases) and non-stone formers(691 cases .Finally 110 cases were enrolled for each arm of the research study 8 cases were lost during follow up in the stone former research group and 6 cases were lost during follow up in non-stone former research group. Among the 102 stone formers, amongst which 18 cases (17.6%) had bilateral stones, 20cases (19.6%) had multiple stones& 4 (3.9%) cases had hydronephrosis.

In harmony with our research study results it was previously revealed and displayed by various research teams a greater risk for gestational DM and hypertensive disorders with pregnancy in women with a past medical history of nephrolithiasis [7,8].

Coe et al. research team of investigators mentioned contradicted with our current research study findings in which they revealed and displayed that stone disease before conception did not impact pregnancy outcomes; on the other hand, this research study involved a cohort of 40 women only .Previous research studies have emerged the finding in which a greater risk of premature delivery in women presenting with symptomatic nephrolithiasis during pregnancy that in part shows similar findings similar to the current research. In which a research study of pregnant women in the Washington state between 1987and 2003, cases that were admitted for management of symptomatic nephrolithiasis had an 80% greater risk of premature delivery another research study of births from 1989 to 2010 at a large obstetric tertiary center symptomatic nephrolithiasis in gestation was correlated with a greater risk of preeclampsia and gestational diabetes [9,10].

Kidney stones are correlated with systemic diseases, involving DM and metabolic syndrome. Obesity is independently correlated with greater risk of renal stone formation, particularly in women. Diabetes is an independent risk factor for occurrence of stones, and stones are a risk factor for occurrence diabetes i.e. a bidirectional correlation. It is hypothesized that insulin resistance causes prolithogenic alterations in urinary composition. In pregnancy, insulin resistance is a normal phenomenon due to raised placentalsecretory levels of diabetogenic hormones, e.g. human chorionic somatomammotropin, corticotrophin releasing hormone growth hormone, and progesterone. Gestational

diabetes occurs when maternal pancreatic functional performance fails in compensation for this normal insulin resistance. One justification is that stone formers develop subclinical insulin resistance before pregnancy that is uncovered by the physiologic normal changes during pregnancy. In a previous research study, the correlation between kidney stone diseases and gestational hypertension risk was most pronounced within obese pregnant women [11-13].

Gillen et al. research team reported 1.7 higher odds of self-reported hypertension outside of pregnancy in cases with a past history of renal stones. Within obese women, both systolic and diastolic BPs were greater in stone formers versus non-stone formers. Furthermore, prior research groups, revealed that stone disease acted as a modifying factor on the correlation between BMI and systolic BP in late gestation [14-16].

Subclinical renal disease is rousingly observed and well known as a risk factor for gestational hypertensive disorders development. Recent research studies have mentioned that cases with congenital solitary kidneys, kidney transplant donors, are at 1.5- to fivefold raised risk for pre-eclamptic development or gestational hypertension emergence .Interestingly renal stone formers could also have subclinical renal functional impairments, even though normal serum creatinine levels are observed [17,18].

In a research series from the Mayo Clinic, asymptomatic stone formers undergoing assessment for living kidney donation were more liable to have renal parenchymal thinning and focal scarring. Subclinical renal injury in the form of either reduced number of nephrons or raised vascular resistance could impair normal renal adaptation to gestation, involving plasma volume expansion, and result in impairment of placental development [19].

The fact raised by some research team's priory that stone formers developed pre-eclamptic disease more frequently but were not more likely to have neonatal complications suggests that the pre-eclampsia that tracks with stone disease is correlated with milder degrees of placental functional distortion. Studies investigating these distinct phenotypes of preeclampsia such as term and preterm according to disease onset have shown that cases that develop preeclampsia after 37 gestational weeks or with a normal angiogenic profile are more liable to be overweight and have comorbid existence of DM. Renal stone formation in these cases could be a marker for underlying endothelial dysfunction, and females who form stones could be more likely to show the clinical issue of preeclampsia disease with milder forms of placental pathology [20].

Hyperuricemia have been linked to both preeclampsia and gestational DM development. Even though uric acid serum levels were similar between stone formers and non-stone formers, this finding was similarly revealed in previous research studies performed. Because the risk of occurrence of renal nephrolithiasis stone disease rises with parity, it is not surprising that a majority of stone formers were multiparous [21].

7. Conclusion

The current research study show that a history of renal stones recognizes females at elevated clinical risk for development of metabolic and hypertensive complications in gestation. This finding supports the linkage between renal nephrolithiasis, DM, and hypertension and recognizes a new cohort that could be variably impacted by renal stones. Furthermore, our research highlights the significance of obesity in its pathophysiological interaction with renal nephrolithiasis and gestational complications. Future research studies are recommended to be multicentric in nature putting in consideration racial and ethnic differences.

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