Pyelonephritis in Pregnancy: Relationship of Fever and Maternal Morbidity

Original Article

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ABSTRACT

Background: Acute pyelonephritis (pyelonephritis or Kidney infection) is accompanied with substantial morbidities for mother and fetus with complications involving preterm labor, preterm delivery, acute renal failures, acute respiratory distress syndromes (ARDS), sepsis, and mother or fetus mortality, in this study; we aimed to assess the association amid maternal fever at the hospitalization admissions and succeeding maternal morbidities in gravid cases with pyelonephritis.

Methods: The current study is a multi-center prospective study. Carried out at obstetrics and gynecology departments of Beni suef University hospitals, Al wasti city hospital and Nasser general hospital in the period between (2019-2021). Cases were allocated into 2 groups, those with and with no fever at the admitting time. Statistical analysis was used to assess the correlation of fever at presentation time with following morbidities. By admission significant symptoms, maternal early warning criteria (MEWC) have been employed and odds ratios estimated to expect intensive care unit (ICU) admissions.

Results: A number of 106 cases have been involved with pyelonephritis in gestation; 50-cases were febrile and 56-cases were nonfebrile on admitting, a high Statistical significance change was found between studied groups as regard Temperature, Heart rate, Respiratory rate and Days in hospital.

Conclusion: Pyelonephritis is accompanied with substantial morbidities for mother and fetus and earlier recognition of those cases at risk can cause improvement in the outcome. Cases with nonfebrile at admittance time are continue at risk of substantial morbidities with comparable admittance rate of ICU, ARDS, pulmonary edema, and preterm birth as febrile cases. Consequently, in cases with clinically signs and urinalysis results indicative of pyelonephritis, even in the nonappearance of fever.

Key Words: ARDS, fever, morbidity, pregnancy, pyelonephritis.

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INTRODUCTION

Acute pyelonephritis (kidney infection) impacts about 1 to 2% of gestations and is one of the main reasons of non-obstetric antenatal hospital-stay. Previous epidemiologic statistics reported a rate of incidence of about 10%, but with enhanced pregnancy surveillance, the occurrence of acute pyelonephritis has reduced lately. But, the progress of anti-biotic resistances and other issues have now influenced the diagnostics, clinical courses, and treatments[1].

Urinary tract infection (UTI) is the commonest bacterial infection throughout gestation. While, symptomless bacteriuria is the commonest shape, acute pyelonephritis is the has the highest rate of prevalent medical complications of pregnancy, that happens in 1 to 2% of all gestations and can cause a vital maternal& fetal morbidities and mortalities. In contrast, pyelonephritis is the main reason of septic shocks in gestation[2].

The symptomless UTI rate of incidence doesn't rise in gestation in comparison to the non-gestation, but physiologic and anatomic variations leading to urinary stasis in gestation rises the clinical disorder risk, particularly in middle gestation and more frequently on the right side of body. American African multi-parous females with the sickle cell trait were reported to have the uppermost occurrence of asymptomatic bacteriuria (ASB). Diagnosing and therapy of ASB, reported in 6% of pregnant women, were found to decrease the risk of pyelonephritis by 70-80 percent[3].

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In pyelonephritis, infections frequently rise from the bladder, because of vesicoureteral reflux in gestation. Further risk factors involving preceding pyelonephritis episodes, urinary tract irregularities or stones and other disorders like diabetes mellitus (DM), sickle cell disorder (SCD), and AIDS[4].

Numerous investigations have concluded motherly and embryonic morbidities accompanying with pyelonephritis. Fever in the 1st trimester throughout organogenesis was accompanying with teratogenicity, miscarriages, and preterm birth. Elevated Uterine activities happens because of the existence of endotoxin and because of the fever as well. The existence of endotoxin is as well supposed to lead to hemolytic anemia in 1/3 of these cases[5].

The current work aimed to assess if fever, precisely at the time of primary assessment, is accompanying with elevated morbidities as showed by ICU admissions. We assumed that those cases with fever at primary presenting time can had raised motherly morbidities. We correspondingly required to evaluate the risks of ARDS, sepsis, preterm delivery, and preterm birth built on fever condition at admissions. Moreover, we evaluated the MEWC utilities at the admittance time to expect a future ICU admittance.

MATERIAL AND METHODS

We attained the ethical committee approval, single-center historical cohort investigation. All cases dis-charged from the gynecology& obstetrics services multi-center prospective study. Carried out at obstetrics and gynecology departments of Beni suef University hospitals, Al wasti city hospital and Nasser general hospital in the period between (2019-2021). Assessed diagnosing involved pyelonephritis in gestation (International Classification of Disorders [ICD]-10 code 0230.00-.03 and ICD-9 code 646.6).

The inclusion criteria were

The age range was from 18 to 50-yrs, and with a clinical diagnosing of pyelonephritis. Those who didn't satisfy these criteria were omitted. The cases have been allocated to 2 groups: cases without a recognized fever in one hour of initial presenting to the room of emergency or labor and delivery election, and cases with a recognized fever in one hour of primary presentations. Fever was described at temperature ≥38°C.

The diagnosing criteria of acute pyelonephritis utilized were flank pains, nausea/vomiting, fever earlier or at admissions, and/or costovertebral angle tenderness, in the existence or nonattendance of cystitis signs. A positive urine culture has been described as >105 CFU/mL of organisms. For cases who had multi-admissions, the data attained was for the 1st admittance.

Sample size

As percent of Positive maternal early warning criteria for pregnant females with fever due to pyelonephritis 41% compared to 15% in pregnant females without fever[6], So sample size is 106. Sample size is calculated using Open Epi program with confidence level 95% and power 80%

The data involving ages, parity, and pregnancy ages built on LMP (last menstrual periods) and ultra-sonography result and existence of UTI were registered in the 1st visit. Throughout admittance, clinical results like fever, chills, flunk pains, costovertebral angle tenderness (one or two-sides) and the recorded blood pressure in addition to laboratory testing findings (involving hematocrit, hemoglobin, urea, urine analysis, urine culture, creatinine, and antibiogram).

Cases' data involving their anti-biotic routine, respond to treatment and urine culture findings reported. The urine culture re-performed 1 or 2-wks thereafter the treatments start. Correspondingly, late pyelonephritis consequences in cases, like pregnancy end, newborn delivery weights and Apgar scoring were also listed.

Further collection of data involves the existence of co-morbid drug disorders like anemia and DM, and pyelonephritis risk factors involving UTI in present gestation, ASB, renal lithiasis, or sexual transmitting infections in existing gestation. Details on significant symptoms from hospital admissions and conscious levels, maximum temp throughout hospital-stay, hospitalization period, ICU admissions, existence of ARDS, and pre-term delivery have been gathered.

Statistical analysis of the data

The collected data have been analyzed via IBM-SPSS-20.0. program (Armonk, NY: IBM Corp).The Kolmogorov- Smirnov test has been utilized to find out the normality of distribution of variables; Comparison among the study groups for categorical variables have been evaluated via Chi-square testing (Fisher's Exact corrections). Student t-testing has been employed to match the studied groups for normally distributed quantitative variables while Mann Whitney testing has been employed to match study groups for quantitative variables with non-normally distribution. Significance of the findings has been considered at the level of 5%.

RESULTS

This table revealed that among Total, the mean of Age was 26.06 (± 3.43 SD), the mean of BMI was 28.16 (± 2.46 SD), the mean of Nulli-parous was 6.36 (± 2.47 SD), according to Parity, 54 (50.9%) were Nulli-parous, 52 (49.1%) were multi-parous. There was high significant

change among studied groups regarding Nulli-parous (Table 1, Figure 1).

Among Fever during hospital course, 5(10.0%) were Anemia, 3(6.0%) were DM, 4(8.0%) were Nephrolithiasis, 5(10.0%) were ASB, 14(28.0%) were UTI during current pregnancy, 4(8.0%) were Recurrent UTI, 0(0.0%) were Prior pyelonephritis, 13(26.0%) were Positive MEWC, 45(90.0%) were Reported fever at home, 20(40.0%) were Positive urine culture, 3(6.0%) were ICU admission, 3(6.0%) were ARDS. Among No Fever during hospital course, 2(3.6%) were Anemia, 4(7.1%) were DM, 2(3.6%) were Nephrolithiasis, 4(7.1%) were ASB, 16(28.6%) were UTI during current pregnancy, 4(7.1%) were recurrent UTI, 3(5.4%) were Prior pyelonephritis, 7(12.5%) were Positive MEWC, 0(0.0%) were Reported fever at home, 31(55.4%) were Positive urine culture, 2(3.6%) were ICU admission, 1(1.8%) were ARDS. A high significant change among studied groups regarding Reported fever at home (Table 2, Figure 2).

Among Fever during hospital course, the mean of Temperature was 37.79 (± 0.87 SD), the mean of Heart rate was 106.1 (± 14.19 SD), the mean of Respiratory rate was 18.06 (± 1.43 SD), the mean of Systolic blood pressure was 116.40 (± 10.45 SD), the mean of Diastolic blood pressure was 72.0 (± 7.56 SD), the mean of Oxygen saturation was 98.92 (± 0.80SD), the mean of Days in hospital was 3.10 (± 0.93SD). Among No Fever during hospital course, the mean of Temperature was 37.04 (± 0.29 SD), the mean of Heart rate was 96.93 (± 7.77 SD), the mean of Respiratory rate was 16.98 (± 0.82 SD), the mean of Systolic blood pressure was 115.18 (± 11.12 SD), the mean of Diastolic blood pressure was 70.36 (± 8.08 SD), the mean of Oxygen saturation was 98.89 (± 0.85SD), the mean of Days in hospital was 2.46 (± 0.50SD). A high significant change was found among studied groups regarding Temperature, Heart rate, Respiratory rate and Days in hospital (Table 3, Figure 3).

Table 1: Comparing among the studied groups regarding demographic data

	Total (n = 106)	Fever during hospital course		*p*
		Fever (n = 50)	No Fever (n = 56)	
Age (years)				
Mean ± SD.	26.06 ± 3.43	26.58 ± 3.17	25.59 ± 3.61	0.138
Median (Min. – Max.)	26 (20 – 32)	27 (20 – 32)	25 (20 – 32)	
BMI (kg/m^2)				
Mean ± SD.	28.16 ± 2.46	28.31 ± 2.48	28.02 ± 2.46	0.550
Median (Min. – Max.)	28.1 (24 – 32)	28.1 (24.6 – 32)	28.05 (24 – 31.8)	
Nulli-parous				
Mean ± SD.	6.36 ± 2.47	5.14 ± 2.70	7.45 ± 1.59	<0.001*
Median (Min. – Max.)	6.5 (1 – 10)	5 (1 – 10)	7 (5 – 10)	
Parity				
Nulli-parous	54 (50.9%)	24 (48.0%)	30 (53.6%)	0.567
Multi-parous	52 (49.1%)	26 (52.0%)	26 (46.4%)	
GA @admission				
Mean ± SD.	22.84 ± 3.75	22.78 ± 3.75	22.89 ± 3.79	0.878
Median (Min. – Max.)	23 (17 – 29)	22. (17 – 29)	23 (17 – 29)	

SD: Standard deviation χ^2: Chi square testing t: Student t-testing U: Mann Whitney testing
p: *p-value* for comparison among the groups of the study *: Statistical significance at $p \leq 0.05$

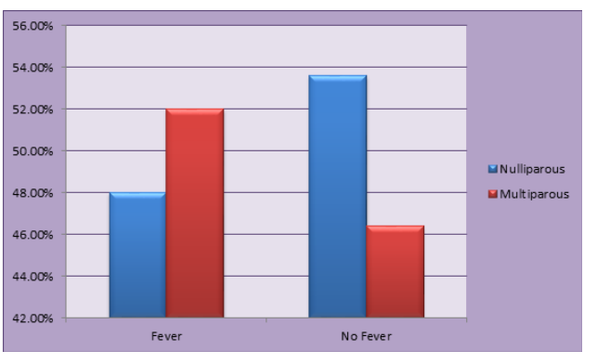

Fig. 1: comparison between fever and no fever according to Parity

Table 2: Comparing among the study groups regarding comorbidities and hospital examination

	Total (n = 106)		Fever during hospital course				*p*
			Fever (n = 50)		No Fever (n = 56)		
	No.	%	No.	%	No.	%	
Anemia	7	6.6	5	10.0	2	3.6	FEp=0.251
DM	7	6.6	3	6.0	4	7.1	FEp=1.000
Nephrolithiasis	6	5.7	4	8.0	2	3.6	FEp=0.418
Asymptomatic bacteriuria	9	8.5	5	10.0	4	7.1	FEp=0.732
Urinary tract infection during current pregnancy	30	28.3	14	28.0	16	28.6	0.948
Recurrent urinary tract infections	8	7.5	4	8.0	4	7.1	FEp=1.000
Prior pyelonephritis	3	2.8	0	0.0	3	5.4	FEp=0.245
Positive maternal early warning criteria	20	18.9	13	26.0	7	12.5	0.076
Reported fever at home	45	42.5	45	90.0	0	0.0	<0.001*
Positive urine culture	51	48.1	20	40.0	31	55.4	0.114
ICU admission	5	4.7	3	6.0	2	3.6	FEp=0.665
ARDS	4	3.8	3	6.0	1	1.8	FEp=0.341

χ^2: Chi square testing FE: Fisher Exact
p: *p-value* for comparison among the groups of the study *: Statistical significance at $p \leq 0.05$

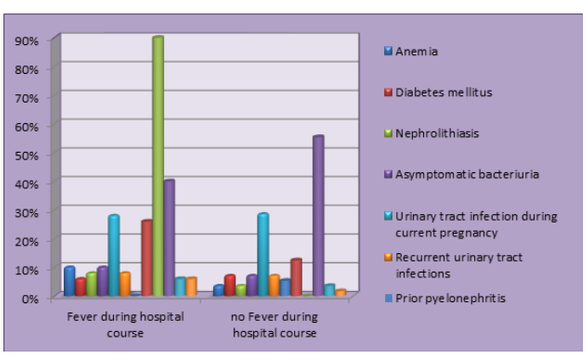

Fig. 2: comparison between fever and no fever according to comorbidities and hospital examination

Table 3: Comparing among the study groups regarding admission hospital examination

Admission Hospital examination	Total (n = 106)	Fever during hospital course		*p*
		Fever (n = 50)	No Fever (n = 56)	
Temp. (°C)				
Mean ± SD.	37.39 ± 0.74	37.79 ± 0.87	37.04 ± 0.29	<0.001*
Median (Min. – Max.)	37.2(36.5 – 39.4)	37.4 (36.6 – 39.4)	37.0 (36.5 – 37.5)	
Heart rate (beats/min.)				
Mean ± SD.	101.3 ± 12.11	106.1 ± 14.19	96.93 ± 7.77	<0.001*
Median (Min. – Max.)	100 (85 – 134)	104 (85 – 134)	98(85 – 110)	
Respiratory rate				
Mean ± SD.	17.49 ± 1.27	18.06 ± 1.43	16.98 ± 0.82	<0.001*
Median (Min. – Max.)	17 (16 – 21)	18 (16 – 21)	17 (16 – 18)	
Systolic blood pressure (mmHg)				
Mean ± SD.	115.75 ± 10.77	116.40 ± 10.45	115.18 ± 11.12	0.563
Median (Min. – Max.)	120 (100 – 130)	120 (100 – 130)	115 (100 – 130)	
Diastolic blood pressure (mmHg)				
Mean ± SD.	71.13 ± 7.85	72.0 ± 7.56	70.36 ± 8.08	0.284
Median (Min. – Max.)	70 (60 – 80)	70 (60 – 80)	70 (60 – 80)	
Oxygen saturation (%)				
Mean ± SD.	98.91 ± 0.82	98.92 ± 0.80	98.89 ± 0.85	0.866
Median (Min. – Max.)	99 (98 – 100)	99 (98 – 100)	99 (98 – 100)	
Days in hospital				
Mean ± SD.	2.76 ± 0.80	3.10 ± 0.93	2.46 ± 0.50	<0.001*
Median (Min. – Max.)	3 (2 – 5)	3 (2 – 5)	2 (2 – 3)	

SD: Standard deviation t: Student t-testing
p: *p-value* for comparison among the groups of the study *: Statistical significance at $p \leq 0.05$

DISCUSSION

Pyelonephritis influences 0.5% of gestations. It is one of the commonest reasons of maternally sepsis, the 3rd main reason of mothers' mortalities universally. In spite of treatments to reduce pyelonephritis in gestation, like ASB screening, the rate of incidence of pyelonephritis has continued stable[6].

This study shows that among fever during hospital course, the mean of Age was 26.58 (± 3.17 SD), the mean of BMI was 28.31 (± 2.48 SD), the mean of Nulli-parous was 5.14 (± 2.70 SD), according to Parity, 24 (48.0%) were Nulli-parous, 26 (52.0%) were multi-parous, the mean of GA @admission was 22.78 (± 3.75 SD). A high significant change was found among studied groups regarding Nulli-parous.

DeYoung *et al*.[6] shows that of the 110-cases satisfying inclusion criteria, 24-cases were febrile on admittance (21.8%) and 86-cases were non-febrile. No changes were found in ages, BMI, nulliparity rate, or racial distributions. The average of pregnancy ages on admissions were 22 and 23.6-wks for the febrile and non-febrile groups.

Sharma *et al*.[7], shows that the cases ages mean was 22 ± 3.41-yrs. A mainstream of patients (74 out of 94 cases, 78.72%) were in the ages range between 20 & 29-yrs. A number of 7034 births at our hospital throughout the investigation's time have been employed for comparisons. The occurrence of gestation with acute pyelonephritis has been reported to be 1.3% (94 out of 7034), that is, 13/1000 births. There were significantly more nulli-parous cases with acute pyelonephritis than the multi-parous cases (75% vs 25%). The mainstream (60.63%) of acute pyelonephritis happened in the 2nd trimester, after that 3rd trimester (31.91%) and 1st trimester (7.44%).

Dawkins *et al*.[1] shows that the mean maternally ages at diagnosing was 24 ± 5.83-yrs, with the mainstream of patients (62 out of 102 cases or 61%) in the ages between 20 and 29-yrs. There were 8-cases (8%) who were with ages>35-yrs (Table 1). 51% of cases were nulli-parous. The patients mainstream of acute pyelonephritis (58.8%) happened in the 2nd trimester, after that 3rd trimester (28.5%) and 1st trimester (14.7%). The mean pregnancy ages at diagnosing were (22 ± 7.8)-wks.

Preceding investigations of pyelonephritis changed in diagnosing criteria, precisely concerning the requirement of fever for the diagnosing. Fever was revealed to have a highly positive prognostic value in pyelonephritis diagnosing. No change in the rate of ICU admittance or

ARDS among cases admitted with a fever in comparison to cases admitted with no fever. Particularly, 3-cases have nonfebrile on admittance eventually need ICU admissions. But all cases who requiring ICU admittance and advanced ARDS were febrile throughout the course of their hospital-stay. This gives indication that even though fever remains a significant clinical condition for the pyelonephritis diagnosing, at the presentation time, this cannot be existing. Therefore, the nonattendance of fever doesn't confirm the nonattendance of upper UTI[8].

This study shows that among fever during hospital course, 5(10.0%) were Anemia, 3(6.0%) were DM, 4(8.0%) were Nephrolithiasis, 5(10.0%) were ASB, 14(28.0%) were UTI during current pregnancy, 4(8.0%) were Recurrent UTI, 0(0.0%) were Prior pyelonephritis, 13(26.0%) were Positive MEWC, 45(90.0%) were Reported fever at home, 20(40.0%) were Positive urine culture, 3(6.0%) were ICU admission, 3(6.0%) were ARDS. A high significant change was found among studied groups regarding Reported fever at home.

DeYoung *et al*.[6] shows that no change was found in the risk factors prevalence among the studied groups. The commonest reported risk factor was preceding UTI in present gestation with 25 and 37.2% rates in the febrile and nonfebrile groups, correspondingly.

Dawkins *et al*.[1] shows that on urinalysis, 81.4% of patients have pyuria, 29.4% were nitrite positive, and 38.2% have microscopic hematuria. The mean hemoglobin at admittance was 10.4 g/dL. 32 cases (30.7%) have hemoglobin of <10 g/dL at admittance and of these, 5 had SCD. 20 cases (19.2%) have absolute white blood cell counts (WBC) >15.0. The median WBC was 12.1 × 109/L ranging from 4.5 to 23.3 × 109/L. There were 17-cases (16.3%) with electrolyte imbalances, but none of cases need ICU admissions.

Hill *et al*.[9] shows that total, 13% of cases have maternally risk factors for antenatal pyelonephritis. The commonest risk factor was pyelonephritis history and ASB. For cases with diabetes-I, the infections mainstream happened in the 1st trimester (*P-value* = .013). When investigated by trimester, nonsignificant changes seen in cases with SCD /trait or previous to pre-term deliveries.

This study shows that among fever during hospital course, the mean of Temperature was 37.79 (± 0.87 SD), the mean of Heart rate was 106.1 (± 14.19 SD), the mean of Respiratory rate was 18.06 (± 1.43 SD), the mean of Systolic blood pressure was 116.40 (± 10.45 SD), the mean of Diastolic blood pressure was 72.0 (± 7.56 SD), the mean of Oxygen saturation was 98.92 (± 0.80SD), the mean of Days in hospital was 3.10 (± 0.93SD). A high significant change was found among studied groups regarding Temperature, Heart rate, Respiratory rate and Days in hospital.

DeYoung *et al*.[6] shows that 18 out of 24 (75%) were febrile cases and 25 (29%) of the 86 nonfebrile cases stated a fever previous to presentations to ER or L&D. Of the nonfebrile cases, 25 (29%) advanced a fever throughout the admittance course. There was no change in rate of positive urine culture among the studied groups. Averagely, cases who were febrile on admittance hospitalized 3-days, whereas nonfebrile cases hospitalized for two-days (p ¼ 0.004). The cases presented with a fever were more frequently to be tachycardic, with heart rate average of 123 beat/min on presentations in comparison to 98 beat/min (*p-value* < 0.001). There were no further clinically significant changes in admittance substantial symptoms among studied groups. But, 12 (50%) of the febrile cases were positive for the MEWC built on their admittance substantial symptoms, while only 9 (10.5%) of the nonfebrile group were positive.

Valent *et al*.[10] shows that the median hospitalizations were 5 (inter-quartile range [IQR]: 5, 7]-days for the extended admittances and 3 (IQR: 2, 4)-days for the predicted average hospital-stay. While ICU admittances (12% in extended group vs. 3% in referent group; p ¼ 0.11) were analogous for the studied groups, extended hospital-stay was accompanying with a higher greatest temp. in the primary 24-h (38.9 [IQR 37.4, 39.5] versus 37.6 [IQR 37.1, 38.8] °C, p ¼ 0.004), raised pulmonary injuries rates (9 versus 0%, p ¼ 0.05), maternally sepsis (20 vs. 3%, *p* ¼ 0.01), and corticoid administrations for fetal advantage at pregnancy ages < 34-wks (16 vs. 3%, p ¼ 0.03).

Restrictions involve the reliance on the electronically medical records for the identifications of cases and data collection. With ICD coding usage, there are concerns that some charts can be inappropriately coded. We accounted for this with detailed review of the medical records to confirm accuracy of the pyelonephritis diagnosing, with elimination of cases with noa clinical pyelonephritis diagnosing in spite of ICD coding. But the opportunity remains that some patients cannot be captured. Our pyelonephritis rate, ARDS, and ICU admittance are all analogous to that has been previously reported. With infrequent opposing events, a bigger sample size can give upgraded capability to measure the prognostic nature of the MEWC scores in expecting maternal morbidities in the basis of pyelonephritis.

CONCLUSION

Pyelonephritis is accompanying with substantial maternally and neonatally morbidity and earlier identifications of those cases at risk may cause enhanced outcome. Cases who are nonfebrile at the time of admittance are still at risk for substantial morbidities with analogous ICU admittance rate, pulmonary edema, ARDS, and preterm birth as febrile cases. Consequently, in cases with clinical signs and urinalysis results expressive of pyelonephritis, even in the nonattendance of fever.

Lastly, we indorse continuing the hospital admittance practice for intra-venous anti-biotics and close observations. Cases with the existence of MEWC are at improved risk of maternal morbidities in the basis of pyelonephritis in gestation; consequently, considerations must be given for raised frequency or levels of monitoring for earlier identifications of worsening in their clinical conditions.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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