The association between urinary tract infection during pregnancy and preeclampsia: A meta-analysis

Ling Yan, MDa, Yu Jin, MDb, Hongdong Hang, MDb,c, Bin Yan, MDb,d,*

Abstract

Objective: The association between urinary tract infection (UTI) during pregnancy and preeclampsia (PE) continues to be the subject of debate. This meta-analysis aimed to examine the relationship between UTI during pregnancy and PE.

Study design: Observational studies up to October 2017, extracted from Medline, PubMed, Cochrane Library, and Embase databases, were included in the analysis. Data were extracted to 4-fold table, and the pooled odds ratio (OR) and 95% confidence intervals (CIs) of respective studies were calculated. Then meta-analysis was performed.

Results: Nineteen studies qualified the inclusion criteria. Urinary tract infection during pregnancy was found to be a risk factor for the development of PE (OR: 1.31, 95% CI: 1.22–1.40).

Conclusion: Occurrence of UTI during pregnancy increases the risk of PE in pregnant women. Screening for, and treatment of UTI should be part of routine antenatal care, especially in developing countries.

Abbreviations: ASB = asymptomatic bacteriuria, AHRQ = Agency for Healthcare research and Quality, CI = confidence interval, DBP = diastolic blood pressure, NOS = Newcastle-Ottawa Scale, OR = odds ratio, PE = preeclampsia, SBP = systolic blood pressure, UTI = urinary tract infection.

Keywords: meta-analysis, preeclampsia, urinary tract infection during pregnancy

1. Introduction

Preeclampsia (PE) is a multisystemic vascular syndrome of pregnancy characterized by hypertension and proteinuria, which typically occurs after 20 weeks of pregnancy. With an estimated incidence of 0.2% to 9.2% in women, PE is a major contributor to maternal and perinatal morbidity and mortality, especially in underdeveloped settings. Although the exact etiology of PE remains unknown, excessive activation of systemic inflammatory response is thought to play a fundamental role in its pathogenesis. It is based on the doctrine that any factor that can provoke the maternal systemic inflammatory response may contribute to the development of PE.

Urinary tract infection (UTI) is a common occurrence during pregnancy with an estimated incidence of approximately 20%. It is thought to play a role in PE by serving to enhance maternal systemic inflammatory response. UTI is also implicated as a contributing factor in other complications such as premature rupture of membranes, preterm birth, low birth weight infant, fetal intrauterine growth restriction, and postpartum endometritis.[1]

A meta-analysis by Conde-Agudelo et al.[2] reported UTI as a risk factor for PE (odds ratio (OR): 1.57, 95% confidence interval (CI) 1.45–1.70) in pregnant women. However, due to the marked heterogeneity between the studies (I² = 79%) included in the meta-analysis, the results should be interpreted cautiously. In addition, several new studies investigating the association of UTI and PE have since been published which requires a fresh evaluation of the available evidence. For example, contradictory results were reported by 2 recently published studies: a multicenter matched control study did not find any definitive evidence of the association between UTI during pregnancy and PE.[3] In contrast, a population-based case-control study reaffirmed the association between maternal UTI and development of PE (OR: 1.22, 95% CI 1.03–1.45).[4]

The main aim of the present study was to evaluate the relationship between UTI during pregnancy and PE by conducting a meta-analysis of relevant observational studies.

2. Materials and methods

Eligible studies up to October 2017 were identified from Medline, PubMed, Cochrane Library, and Embase databases. The following algorithm was employed for the literature search, in abstract or in full-text words: (preeclampsia OR pregnancy hypertension OR hypertensive disorders of pregnancy OR pregnancy-induced hypertension OR gestosis OR gestational...
hypothesis OR pregnancy-associated hypertension OR pregnancy toxemia) and (urinary tract infection OR cystitis OR pyelonephritis OR bacteriuria). The retrieved studies were independently screened by 2 reviewers (LY and YJ). Any disagreement pertaining to the inclusion or exclusion of studies was resolved by consensus among the reviewers. Data extraction from the included studies was performed independently by 2 reviewers (LY and YJ), who were blinded to each other, and subsequently cross-checked all the extracted data. Any disagreement was resolved by consensus. The other 2 authors were responsible for modification of the article (HH and BY). The inclusion criteria were observational studies that investigated the relationship between PE and UTI during pregnancy; use of objective diagnostic criteria for PE: a multisystemic syndrome during pregnancy, characterized by hypertension [defined as systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg, or, a rise of 15 mm Hg in SBP and/or 30 mm Hg in DBP]; and proteinuria occurring after 20 weeks of gestation. Proteinuria was defined as urinary protein excretion ≥0.3 g/24 h, or, random urine specimen with ≥1+ by dipstick, or ≥3 g/L; objective diagnostic criteria for UTI, including bacteriuria and symptomatic UTI; studies published in English language; studies that reported relative risks (RRs) or ORs, or, studies for which the original data set, through which OR could be calculated, was accessible. Case reports, literature reviews, secondary analysis, and studies for which the original dataset were not accessible, were excluded.

The following data were extracted from the studies: general information: author details, year of publication, and geographic catchment area of the study; basic elements of the study: methodology, study groups, sample size, confounding factors, time of pregnancy test, main findings; characteristics of subjects: maternal age, race, socioeconomic and educational status, parity, and body mass index; study outcomes reported as unadjusted and/or adjusted RRs or odds ratio (ORs) and 95% CIs. Studies were evaluated using the Newcastle-Ottawa Scale (NOS) for quality assessment of case-control and cohort studies. In addition, the cross-sectional studies were evaluated by the Agency for Healthcare research and Quality (AHRQ). Those studies with ≥5 points were thought to be of high quality.

Heterogeneity among the results of studies was assessed with the Cochran Q statistic, which included qualitative P value and quantitative I². Begg test was performed to detect publication bias. Data analyses employed the most adjusted OR and 95% CI for the studies included. Results obtained from different studies were combined to produce a pooled OR with 95% CI. Finally, sensitivity analysis was performed by sequential exclusion of 1 study at a time. All statistical analyses were performed with Stata 12.0.

2.1. Ethical approval and consent from patients

The project was not primary research involving humans or animals but was an analysis of human subject data available in the public domain; and thus no ethical approval and patient consent were required.

3. Results

3.1. Study selection

The literature search yielded 734 citations. After elimination of duplicate citations, the full texts of studies were reviewed by authors (LY and YJ). Only 19 studies met the inclusion criteria (Fig. 1); 5 studies were excluded according to the inclusion criteria and exclusion criteria. Of the 19 studies, 14 studies (6 cohort; 1 cross-sectional study; 7 case-control studies) indicated UTI during pregnancy as a risk factor for PE; the other 5 studies (both cohort and case-control studies) did not reveal any association between the 2 (Table 1). As rated on the NOS and AHRQ scale, all 19 studies scored ≥5 points, which attested to their high quality. The possibility of publication bias was assessed with Begg test (P = .208); the results showed no obvious effect of publication bias on our analysis.

3.2. The relationship between UTI during pregnancy and preeclampsia

Overall, the pooled OR with fixed-effects model was 1.31 (95% CI: 1.22–1.40) (Fig. 2), which indicates UTI during pregnancy as a risk factor for development of PE. In other words, the ratio of UTI to non-UTI in PE is 1.31 times than that of non-PE. A low level of heterogeneity was observed among the studies in this respect (I² = 36.8%, P = .55). On subgroup analysis, differences with respect to sample size and economic level of subjects were the main sources of heterogeneity, because the pooled ORs were not similar to the overall pooled OR (Table 2).

3.3. Subgroup and sensitivity analysis

Subgroup analyses were performed based on sample size, study design (cohort or cross-sectional study vs case-control), economic level (developed countries vs developing countries) and whether adjustment was performed for body weight or parity. Table 2 shows the detailed results. On subgroup analysis, studies conducted in developing countries were found to be associated with a higher pooled OR (OR: 3.03, 95% CI 1.87–4.19) as compared to that of studies conducted in developed countries (OR: 1.30, 95% CI 1.21–1.39). In addition, adjustment for body weight and parity had no influence on the results (Table 2).

Sensitivity analysis of the observed association between urinary tract infection and PE was performed. The results showed that exclusion of any individual study had little influence on the pooled OR (95% CI) (Fig. 3).

4. Discussion

4.1. Relationship between UTI during pregnancy and preeclampsia

There are lingering questions regarding the nature of association between maternal infection and PE. Indeed the relationship between UTI during pregnancy and PE has evoked much debate in the last 40 years. In the absence of any definitive evidence, the precise nature of the association, whether casual, confounded, or spurious, is yet to be elucidated. The subject of our research is important as UTI is a common occurrence in pregnant women, and can be easily diagnosed and effectively treated. Detection of an association between UTI in pregnancy and PE could help devise interventions for early diagnosis and treatment of UTI, which would ameliorate a major cause of complication in pregnant women.

Our study suggests that UTI during pregnancy had 1.31-fold higher risk of PE. Minassian et al. also found that pregnant women with UTI were more likely to develop PE in mid-pregnancy. Moreover, results from 2 nonrandomized clinical
trials from Germany\textsuperscript{24} and Croatia\textsuperscript{25} suggest that antibiotic treatment for bacteriuria could significantly reduce the incidence of PE (OR: 0.22, 95% CI: 0.17–0.30 and OR: 0.36, 95% CI: 0.20–0.64, respectively), as compared to that in pregnant women with untreated bacteriuria. Furthermore, a prospective cohort study in 2013 claimed that pregnant women with asymptomatic bacteriuria (ASB) (32–34 weeks of gestation) were at a 3.79 times higher risk of developing PE as compared to pregnant women without ASB; however, no significant difference was seen in early screening and treatment of UTI (till 20 weeks of gestation) between the 2.\textsuperscript{6} Overall, these findings imply that early screening and treatment of UTI can reduce the incidence of PE.

In addition, our subgroup analysis revealed that pregnant women with UTI in developing countries were at an increased risk of PE as compared to their counterparts in developed countries. This appears to be due to better quality of antenatal care in the developed countries that includes regular screening for UTI.

Furthermore, obesity and primiparity are known high risk factors for PE. In our subgroup analysis, adjustment for body weight and parity had no influence on the results.

4.2. Pathogenesis
The pathogenesis of PE remains unclear so far, despite decades of research. The pathophysiology of PE is believed to involve aberrant placentation and systemic inflammation. In a study by LaMarca et al\textsuperscript{26} inflammatory responses in preeclamptic pregnancies was found to be excessive as compared to that in normal pregnancies. Uteroplacental atherosis is known to be directly associated with PE. Moreover, inflammatory response plays an important role in the initiation and enhancement of uteroplacental atherosis. Therefore, it is plausible that infectious disease, which increase systemic inflammatory burden would also increase the risk of PE. During pregnancy, UTI is one of the most common maternal infections, which can potentially lead to activation of systemic inflammatory response and endothelial injury; this in turn can lead to placental hypoxia and uteroplacental atherosis, and eventual development of PE.

4.3. Strengths and limitations
This study reveals the relationship between UTI during pregnancy and PE through meta-analysis, which is relatively
| First author, year | Region, country | Design | Study groups | N   | Confounding factors | Time of pregnancy test | Main findings                                                                 | Quality assessment |
|-------------------|----------------|--------|--------------|-----|---------------------|------------------------|-----------------------------------------------------------------------------|--------------------|
| Love, et al, 1964[41] | Canada         | Cohort | Women with UTI | 80  | None                | At first antenatal visit | No association between asymptomatic bacteriuria and pre-eclampsia            | 5 Points           |
|                    |                |        | Women without UTI | 394 |                     |                         |                                                                            |                    |
| Stuart, et al, 1965[42] | Jamaica       | Prospective cohort | Women with UTI | 88  | None                | Not reported            | Bacteriuria was a risk factor for pre-eclampsia                            | 6 Points           |
|                    |                |        | Women without UTI | 729 |                     |                         |                                                                            |                    |
| Kincad-Smith et al 1965[41] | Australia | Case control | Women with UTI | 240 | None                | At first antenatal visit | Bacteriuria was a risk factor for pre-eclampsia                            | 5 Points           |
|                    |                |        | Women without UTI | 500 |                     |                         |                                                                            |                    |
| Little, 1966[10] | United Kingdom | Prospective cohort | Women with UTI | 269 | None                | 12 weeks                | No association between bacteriuria and pre-eclampsia                       | 7 Points           |
|                    |                |        | Women without UTI | 4735|                     |                         |                                                                            |                    |
| Savidge et al, 1983[17] | Australia     | Case control | Women with PE | 51  | None                | At delivery              | Bacteriuria was a risk factor for pre-eclampsia                           | 6 Points           |
|                    |                |        | Women without PE | 72  |                     |                         |                                                                            |                    |
| Gilbert et al, 1986[13] | Melbourne     | Case-control | Women with PE | 51  | None                | The first trimester      | UTI† was a risk factor for pre-eclampsia                                  | 6 Points           |
|                    |                |        | Women without PE | 1182|                     |                         |                                                                            |                    |
| Hill et al, 1986[16] | Australia     | Case-control | Women with PE | 100 | Age, number of vaginal examination | At delivery               | Asymptomatic bacteriuria was a risk factor for pre-eclampsia               | 6 Points           |
|                    |                |        | Women without PE | 200 |                     |                         |                                                                            |                    |
| Schieve et al, 1994[7] | Chicago, IL   | Retrospective cohort | Women with UTI | 1988| Age, race, outcome of previous pregnancy, genital infection, hospital births | Not reported                        | UTI† was a risk factor for pre-eclampsia                                  | 7 Points           |
|                    |                |        | Women without UTI | 23,758|                     |                         |                                                                            |                    |
| Qureshi et al, 1996[18] | Karachi, Pakistan | Prospective cohort | Women with UTI | 77  | None                | 17.3 ± 10.1 weeks        | No association between bacteriuria and pre-eclampsia                       | 7 Points           |
|                    |                |        | Women without UTI | 1520|                     |                         |                                                                            |                    |
| Mitterndorff et al, 1996[10] | Boston, MA | Case-control | Women with PE | 386 | Age, parity, education, BMI, economic status, infant sex, pregnancy weight gain, hemorrhage | Not reported                  | UTI† was a risk factor for pre-eclampsia                                  | 8 Points           |
|                    |                |        | Women without PE | 2355|                     |                         |                                                                            |                    |
| Lee, et al, 2000[18] | Taiwan        | Retrospective cohort | Women with PE | 415 | Age, parity, BMI, economic status, education, multiple births | Not reported                  | UTI† was a risk factor for pre-eclampsia                                  | 7 Points           |
|                    |                |        | Women without PE | 29,320|                     |                         |                                                                            |                    |
| Ullah et al, 2000[20] | Bangladesh     | Cross-sectional | Women with UTI | 134 | Parity, economic status | Second trimester          | UTI† was a risk factor for pre-eclampsia                                  | 8 Points           |
|                    |                |        | Women without UTI | 134 |                     |                         |                                                                            |                    |
| Mazor-Dray et al, 2009[18] | Negev, Israel | Retrospective cohort | Women with UTI | 4742| Age, parity | 12-13 weeks                | UTI† was a risk factor for pre-eclampsia                                  | 6 Points           |
|                    |                |        | Women without UTI | 1,099,033 |                     |                         |                                                                            |                    |
| Bihmody et al, 2007[17] | Hungary         | Retrospective cohort | Women with UTI | 2188| Age, parity | 6-12 weeks or 4 or 7 months | UTI† was a risk factor for pre-eclampsia                                  | 7 Points           |
|                    |                |        | Women without UTI | 35,963|                     |                         |                                                                            |                    |
| Minassian et al, 2013[3] | United Kingdom | Case-control | Women with PE | 1533| Age, BMI, previous hypertension/diabetes mellitus/renal disease, multiple pregnancy | Any time in pregnancy           | UTI† was a risk factor for pre-eclampsia                                  | 7 Points           |
|                    |                |        | Women without PE | 14,236|                     |                         |                                                                            |                    |
| Jain et al, 2013[19] | North India    | Prospective cohort | Women with UTI | 58  | Age, parity, anemia, living conditions | 32-34 weeks                | UTI† was a risk factor for pre-eclampsia                                  | 8 Points           |
|                    |                |        | Women without UTI | 44  |                     |                         |                                                                            |                    |
| Kazemir et al, 2015[20] | Netherlands | Prospective cohort | Women with UTI | 208 | Smoking, education, assisted reproductive technology | 16-22 weeks                | UTI† was a risk factor for pre-eclampsia                                  | 8 Points           |
|                    |                |        | Women without UTI | 4035|                     |                         |                                                                            |                    |
| Rezavand et al, 2015[20] | Kerman, Iran | Case-control | Women with PE | 125 | Age, parity | Third trimester          | UTI† was a risk factor for pre-eclampsia                                  | 7 Points           |
|                    |                |        | Women without PE | 125 |                     |                         |                                                                            |                    |
| Izudneau et al, 2017[21] | Nigeria       | Prospective cohort | Women with UTI | 65  | None                | 23 ± 2.1 weeks            | No association between UTI† and pre-eclampsia                             | 7 Points           |
|                    |                |        | Women without UTI | 65  |                     |                         |                                                                            |                    |

BMI = body mass index; PE = pre-eclampsia; UTI = urinary tract infection.

† UTI included both asymptomatic and symptomatic urinary tract infections.
‡ UTI included asymptomatic bacteriuria.
§ UTI included both asymptomatic and symptomatic urinary tract infections.
\* UTI included asymptomatic bacteriuria due to ureaplasmas and other fastidious organisms.
innovative. In addition, our findings are more reliable than those of the meta-analysis by Conde-Agudelo et al\textsuperscript{(2)}, owing to the low level of heterogeneity in our study. However, our meta-analysis also has several limitations. We restricted the scope of our meta-

Figure 2. Forest plots for overall results and heterogeneity test of the meta-analysis. The pooled odds ratio (OR) was 1.31 (95% CI: 1.21–1.41), which indicates urinary tract infection (UTI) during pregnancy as a risk factor for development of preeclampsia. And there was a low heterogeneity among the studies ($\textit{I}^2=36.8\%$). CI = confidence interval.

| Subgroup                                      | No. studies | $P$ ($\chi^2$) | Pooled odds ratio (95% CI) |
|-----------------------------------------------|-------------|----------------|----------------------------|
| Study design                                  |             |                |                            |
| Cohort or cross-sectional                     | 12          | .377 (7.0%)    | 1.31 (1.21–1.41)           |
| Case-control                                  | 7           | .011 (64.0%)   | 1.31 (1.12–1.51)           |
| Economic level                                |             |                |                            |
| Developed countries                           | 12          | .166 (28.5%)   | 1.30 (1.21–1.39)           |
| Developing countries                          | 7           | .596 (0.0%)    | 3.03 (1.87–4.10)           |
| Sample size                                   |             |                |                            |
| $<$100 Women with preeclampsia               | 8           | .300 (16.5%)   | 2.16 (1.51–2.81)           |
| $\geq$100 Women with preeclampsia            | 11          | .201 (25.5%)   | 1.29 (1.20–1.39)           |
| Adjustment for body weight                    |             |                |                            |
| No                                            | 16          | .037 (42.6%)   | 1.33 (1.22–1.43)           |
| Yes                                           | 3           | .371 (0.0%)    | 1.25 (1.05–1.46)           |
| Adjustment for parity                         |             |                |                            |
| No                                            | 13          | .076 (38.0%)   | 1.3 (1.18–1.42)            |
| Yes                                           | 6           | .055 (36.8%)   | 1.33 (1.18–1.48)           |

CI = confidence interval, UTI = urinary tract infection.
prepregnancy obesity, and primiparity are known risk factors for PE. The lack of adjustment for these confounding factors may have slightly overestimated the OR. Finally, because of a lack of randomized controlled trials, we had to consider only observational studies, which inevitably led to clinical heterogeneity as compared to that associated with double-blind randomized controlled trials.

To conclude, results of our meta-analysis are consistent with those of previous studies which have implicated UTI as a risk factor for the development of PE in pregnant women. Furthermore, it lends credence to the importance of screening for, and treatment of, UTI in pregnant women, especially in developing countries. However, due to its nature, meta-analysis is vulnerable to several forms of bias which may get introduced during the stage of literature search, retrieval, review, and/or data extraction. Randomized controlled trials with robust methodology, and which take cognizance of the timeline of events, dose-response association, and the treatment effects are required to confirm the relation between UTI and PE of pregnancy.

Acknowledgments
The authors thank The First Affiliated Hospital of Xiamen University, The First Affiliated Hospital of Dalian Medical University, and No. 210 Hospital of PLA during the preparation of the manuscript. We also appreciate the Medjaden Bioscience Limited for their edit and proofreading.

Author contributions
Conceptualization: Ling Yan, Hongdong Hang, Bin Yan.
Data curation: Hongdong Hang, Bin Yan.
Formal analysis: Ling Yan, Yu Jin, Bin Yan.
Funding acquisition: Ling Yan, Yu Jin.
Investigation: Ling Yan, Yu Jin.
Methodology: Yu Jin.
Resources: Bin Yan.
Supervision: Ling Yan, Hongdong Hang, Bin Yan.
Validation: Hongdong Hang, Bin Yan.
Visualization: Bin Yan.
Writing – original draft: Ling Yan, Bin Yan.

References
[1] Christensen B. Which antibiotics are appropriate for treating bacteriuria in pregnancy? J Antimicrob Chemother 2000;46(suppl A):29–34.
[2] Conde-Agudelo A, Villar J, Lindheimer M. Maternal infection and risk of preeclampsia: systematic review and metaanalysis. Am J Obstet Gynecol 2008;198:7–22.
[3] Shamsi U, Hatcher J, Shamsi A, et al. A multicentre matched case control study of risk factors for preeclampsia in healthy women in Pakistan. BMC Womens Health 2010;10:14.
[4] Minassian C, Thomas SL, Williams DJ, et al. Acute maternal infection and risk of pre-eclampsia: a population-based case-control study. PLoS One 2013;8:e73047.
[5] Banhidy F, Acs N, Puho EH, et al. Pregnancy complications and birth outcomes of pregnant women with urinary tract infections and related drug treatments. Scand J Infect Dis 2007;39:390–7.
[6] Jain V, Das V, Agrawal A, et al. Asymptomatic bacteriuria and obstetric outcome following treatment in early versus late pregnancy in north Indian women. Indian J Med Res 2013;137:753–8.
[7] Schieve LA, Handler A, Hershov R, et al. Urinary tract infection during pregnancy: its association with maternal morbidity and perinatal outcome. Am J Public Health 1994;84:403–10.
[8] Lee CJ, Hsieh TT, Chiu TH, et al. Risk factors for pre-eclampsia in an Asian population. Int J Gynaecol Obstet 2000;70:327–33.
[9] Mazor-Dray E, Levy A, Schlaeffer F, et al. Maternal urinary tract infection: is it independently associated with adverse pregnancy outcome? J Matern Fetal Neonatal Med 2009;22:124–8.
[10] Stuart KL, Cummins GT, Chin WA. Bacteriuria, prematurity, and the hypertensive disorders of pregnancy. Br Med J 1965;1:554–6.
[11] Rathod KB, Joswal KN, Sreerastava AC, et al. Study of placenta in sickle cell disorders. Indian J Pathol Microbiol 2007;50:698–701.
[12] Mittendorf R, Lain KY, Williams MA, et al. Preeclampsia. A nested, case-control study of risk factors and their interactions. J Reprod Med 1996;41:491–6.
[13] Gilbert GL, Garland SM, Fairley KF, et al. Bacteriuria due to ureaplasmas and other fastidious organisms during pregnancy: prevalence and significance. Pediatr Infect Dis 1986;5:425–43.
[14] Hill JA, Devoe LD, Bryans CJ Jr. Frequency of asymptomatic bacteriuria in preeclampsia. Obstet Gynecol 1986;67:529–32.
[15] Kincad-Smith P, Bullen M. Bacteriuria in pregnancy. Lancet 1965;1:395–9.
[16] Rezavand N, Vesi F, Zangane M, et al. Association between asymptomatic bacteriuria and pre-eclampsia. Glob J Health Sci 2015;8:235–9.
[17] Savij A, Gilbert GL, Fairley KF, et al. Bacteriuria due to Ureaplasma urealyticum and Gardnerella vaginalis in women with preeclampsia. J Infect Dis 1983;148:605.
[18] Kazemier BM, Koningstein FN, Schneeberger C, et al. Maternal and neonatal consequences of treated and untreated asymptomatic bacteriuria in pregnancy: a prospective cohort study with an embedded randomised controlled trial. Lancet Infect Dis 2015;15:1324–33.
[19] Little PJ. The incidence of urinary infection in 5000 pregnant women. Lancet 1966;2:925–8.
[20] Qureshi RN, Khan KS, Darr O, et al. Bacteriuria and pregnancy outcome: a prospective hospital-based study in Pakistani women. J Pak Med Assoc 1994;44:12–3.
[21] Izuchukwu KE, Oranu EO, Bassey G, et al. Maternofetal outcome of asymptomatic bacteriuria among pregnant women in a Nigerian Teaching Hospital. Pan Afr Med J 2017;27:69.
[22] Low JA, Johnston EE, McBride RL, et al. The significance of asymptomatic bacteriuria in the normal obstetric patient. Am J Obstet Gynecol 1964;90:897–906.
[23] Ullah MA, Barman A, Siddique MA, et al. Prevalence of asymptomatic bacteriuria and its consequences in pregnancy in a rural community of Bangladesh. Bangladesh Med Res Counsc Bull 2007;33:60–4.
[24] Fischer W, Lamm D, Bayer H, et al. Correlation between urinary tract infection and pregnancy toxemias [in German]. Zentralbl Gynakol 1970;92:1326–33.
[25] Drazanic A, Balasa A, Zadilovic J, et al. The effect of treatment of bacteriuria on pregnancy outcome [in Croatian]. Jugosl Ginekol Perinatol 1989;29:15–8.
[26] LaMarca BD, Ryan MJ, Gilbert JS, et al. Inflammatory cytokines in the pathophysiology of hypertension during preeclampsia. Curr Hypertens Rep 2007;9:480–5.