Assessment of Biochemical Changes in Pregnancy Induced Hypertension (PIH) among Saudi Population at KAMC-Riyadh

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Authors’ contributions

This work was carried out in collaboration between all authors. Author TK was the principal investigator of the research project, responsible for designing of the entire work. Authors TK, MAF and WAT were responsible for the entire write up. Authors KROA, MJA and FMSA were responsible for data collection. Authors IAH, SG and IA were responsible for the data management. Author SQ assisted in writing and attending to comments of the referees and rewriting some parts of the manuscript. He was responsible to correspond with the journal. All authors read and approved the final manuscript.

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ABSTRACT

**Background:** One of the most common complications that affect around 2-5% pregnant women is elevated blood pressure defined as gestational hypertension.

**Aims & Objective:** To compare and correlate between plasma urea, creatinine, sodium, potassium, and plasma glucose and urine protein in pre-eclamptic and normotensive groups.

**Materials and Methods:** This is quantitative retrospective chart review study. It is an hospital based case control study involving data from 199 age – matched Saudi women, discharged from Obstetrics and Gynecology Department of King Abdul Aziz medical city during the period of 2013-2014. The data were collected following standard procedures and statistical analysis was done using independent t – test and correlation.

**Results:** The levels urea, creatinine, sodium, potassium in the serum, plasma glucose and urine protein were significantly elevated in pre-eclamptic women when compared to normotensives ($p=0.000$, $p=0.000$, $p=0.005$, $p=0.000$, $p=0.000$, $p=0.000$ respectively). There was a significant positive correlation between urea and protein, urea and creatinine ($r=0.3$ $P=0.002$), ($r=0.7$ $p=0.000$) respectively.

**Conclusion:** The elevated values of serum creatinine, urea, urine protein, sodium, potassium and plasma glucose preclude them to be useful for consideration as consistent predictive indicator(s) for pre-eclampsia or pregnancy related hypertension.

**Keywords:** Preeclampsia; proteinuria; obstetrics; gynecology; normotensive.

1. INTRODUCTION

One of the most common complications that affect 2-5% pregnant women is elevated blood pressure defined as gestational hypertension. Increased blood pressure usually starts after the 20th week of gestation without proteinuria [1,2]. Pregnancy-induced hypertension (PIH), which occurs in <10% of pregnancies, is a major risk factor for maternal and perinatal morbidity and mortality. PIH includes gestational hypertension as well as pre-eclampsia and eclampsia [3,4]. Measurement of blood pressure and proteinuria should be routine investigation during entire period of gestation [5].

Unfittingly implanted placenta is suggested as the main reason of gestational hypertension in pregnant women. Consequently correctly embedded placenta facilitates best transferring of oxygen from mother to fetus; otherwise failure in proper growth of placenta in uterus leads to development of pre-eclampsia and eclampsia [6,7]. Moreover a pregnant woman may have intercurrent diseases associated with gestational hypertension, that may become worse and be a potential risk to the pregnancy.

PIH causes important changes of biochemical parameters such as increased levels of blood glucose, urea, creatinine, uric acid, transaminases, lactate dehydrogenase and increased level of proteinuria with hypoalbuminemia which are used as indicator of disease severity. Biochemical changes also include alteration of lipid level, because hypertension is associated with peripheral vascular diseases, so gestational hypertension appears to be crucial justification in changes of lipid [8].

There is a paucity of literature on PIH from Riyadh, Saudi Arabia, hence the present study was undertaken to compare and correlate the biochemical changes that arise from PIH and early detection of these changes offer chance to avoid complications.

2. MATERIALS AND METHODS

2.1 Study Design

This is quantitative retrospective chart review, an hospital based case control study.

2.2 Study Area and Duration

This study was conducted in King Abdul-Aziz Medical City (KAMC) complex in Riyadh, Saudi Arabia, during the period from September 2015 to November 2015.

2.3 Study Subjects

One hundred and ninety nine pregnant women were selected from all women who attended obstetrics department from 2013-2014; they were categorized into two groups according to the following criteria:
2.3.1 Inclusion criteria

The first group included pregnant women of all ages with a diagnosis of pre-eclampsia, while the control group included pregnant women without gestational hypertension.

2.3.2 Exclusion criteria

Women diagnosed with hypertension or diabetes mellitus before pregnancy were excluded. Women diagnosed with gestational diabetes were also excluded from the second group.

2.3.3 Sample size

The sample size is 199 subjects based on previous auditing institutional report and on the calculated prevalence of gestational hypertension in Riyadh region.

The sample size and confidence level computed were 200 and 95% respectively.

2.4 Sampling Technique

The sample included pregnant women of different age groups discharged from KAMC-CR with diagnosis of gestational hypertension and other groups of pregnant women without gestational hypertension, at any point in time during 2013 and 2014. Blood and urine samples from both the study groups, pre-eclamptic and normotensive women were collected after 20th week of pregnancy within second trimester.

2.5 Ethical Consideration

Patient’s confidentiality was strictly observed throughout the study by using Medical Record Number. Data access was restricted to the investigators. The study was approved by Institutional Review Board of King Abdullah International Medical Research Center, National Guards, Riyadh.

2.6 Data Management and Analysis Plan

All information and data collected from the patients was entered into Excel file. A backup soft copy as well as a hard copy was dated, saved and secured after each data entry update. A designated study binder and a dedicated USB flash memory were kept with the principal investigator.

2.7 Statistical Analysis

Statistical analysis of study variables was carried out using SPSS software. Descriptive and demographic data was expressed as mean ± standard deviation and percentage. Independent t and correlation tests were used, wherever applicable.

3. RESULTS

This study was conducted on 149 pregnant women diagnosed with pre-eclampsia as the test group and 50 women with normal pregnancy as control group. Age of the test group was matched with the control group. In the present study 14.8% (n=22) of the test group was diagnosed with severe pre-eclampsia and 85.2% (n=127) of the test group was diagnosed with moderate pre-eclampsia as illustrated in Fig. 1.

![Fig. 1. Frequency of severe and moderate pre-eclampsia among all patients](image)

3.1 Independent t-test

Table 1 Comparison of means of serum levels of urea, Creatinine, Sodium, Potassium, Plasma Glucose and urine protein was done between test and control groups. Table 2 Comparison of means of serum levels of urea, Creatinine, Plasma Glucose and urine protein between types of pre-eclampsia against test.

3.2 According to Correlation Analysis

Fig. 2 shows moderate positive correlation between levels of urea in mmol/l and levels of protein in mg/dl (r=0.3 P=0.002).

Fig. 3 shows strong positive correlation between levels of urea in mmol/l and levels of creatinine in µmol/l(r=0.7 P=0.000).

Fig. 4 shows moderate positive correlation between levels of urea in mmol/l and levels of potassium in mmol/l(r=0.3 P=0.001).
Table 1. Comparison of means of serum levels urea, creatinine, sodium, potassium, plasma glucose and urine protein between test and control group

| Variable  | Test (n=149) | Control (n=50) | p value |
|-----------|--------------|----------------|---------|
| Urea      | 3.7±1.6      | 2.2±0.6        | 0.000   |
| Creatinine| 57.72±18.69  | 46.68±5.426    | 0.000   |
| Sodium    | 135.54±1.761 | 136.34±1.636   | 0.005   |
| Potassium | 4.221±3989   | 3.928±3064     | 0.000   |
| Glucose   | 5.419±1.7405 | 4.590±0.7413   | 0.000   |
| Protein   | 348±50       | 19.10±9.9      | 0.000   |

The table shows the mean ± standard deviation and probability (P).

P value ≤ 0.05 is considered significant

Table 2. Comparison of means of serum levels of urea, creatinine, plasma glucose and urine proteins between types of pre-eclampsia against test

| Variable  | Severe preeclampsia (n=127) | Moderate preeclampsia (n=22) | p value |
|-----------|-----------------------------|-----------------------------|---------|
| Glucose   | 5.6±1.8                     | 4.6±1.1                     | 0.003   |
| Protein   | 385±53                      | 136±31                      | 0.000   |
| Urea      | 3.8±1.7                     | 3.5±1.7                     | 0.223   |
| Creatinine| 57.7±20.                    | 57.7±6.4                    | 0.990   |

The table shows the mean ± standard deviation and probability (P).

P value ≤ 0.05 is considered significant

Fig. 2. A scatter plot shows the correlation between serum levels of urea in mmol/l and urine levels of protein in mg/dl (r=0.3 p=0.002)

4. DISCUSSION

Being given to understand that proteinuria is an important sign of pre-eclampsia and the minimum criteria for the diagnosis of pre-eclampsia are hypertension plus proteinuria [9] it is recommended that urinary dipstick testing (visual or automated) may be used for screening of proteinuria when the suspicion of preeclampsia is low [10]. Accordingly results of present study revealed significant increase in proteinuria in preeclamptic women compared with normotensive women. Furthermore our results observed significant increase in proteinuria among pregnant women diagnosed with severe pre-eclampsia compared with pregnant women diagnosed with moderate preeclampsia. This observation is supported by the known criteria for diagnosis of severe preeclampsia [11] where the increase of BP (< 140 systolic and < 90 diastolic) and proteinuria (0.3 g/day) after 24 week of gestation.

Fig. 3. A scatter plot shows the correlation between serum levels of urea in mmol/l and creatinine in µmol/l (r=0.7 p=0.000)

Fig. 4. A scatter plot shows the correlation between serum levels of urea in mmol/l and potassium in mmol/l (r=0.3 p=0.001)
Creatinine and urea are non-protein nitrogenous metabolites that are removed from the body by the kidney through glomerular filtration and also used as indicators of kidney function and other conditions. Although measurement of urea and creatinine may have little value in the prediction of preeclampsia, estimation of these parameters in serum during pregnancy helps to diagnose kidney function especially at women with preeclampsia signs [12]. Previous study by Egwuatu et al. [13] showed increased creatinine level in preeclamptic women. Furthermore Magna and Sitikantha [8] also observed significant elevation in serum creatinine and small insignificant increase in serum urea level in pre-eclamptic when compared to normotensive women. These studies support our observation on the significant increase in serum urea and creatinine in pregnant women with pre-eclampsia compared to normotensive pregnant women, besides lack of correlation between urea and creatinine level and severity of eclampsia for both.

It is a well-known fact that electrolytes play an important role in the pathogenesis of hypertension. Dietary sodium restriction is one of the prime treatments of high blood pressure [14]. Therefore estimation of serum electrolytes in PIH provides a very useful index for the study of physiological and pathological changes during pregnancy. In the present study, a significant decrease in plasma sodium levels was seen in the preeclamptic patient compared to normotensive. Our findings are in accordance with those reported by others [14,15].

Sodium transport is altered across the cell membrane and this leads to the accumulation of sodium in the extravascular spaces and a decrease in the plasma sodium levels. The serum sodium levels tend to decline in cases of preeclampsia as the disorder increases in severity [15]. These studies corroborates our observation on the significant increase in the serum levels potassium in PIH cases as compared to that in the normal normotensive pregnant. However; these results are not in accordance with the observation of Indumati et al. [14]. Hence, this increase might be due to renal impairment or using of corticosteroid therapy during pregnancy.

Results of present study demonstrated significant increase in blood glucose in preeclamptic women compared to normotensive. These results confirm a previous study which observed that a minor degree of glucose intolerance is associated with a higher occurrence of preeclampsia in non-diabetic pregnant women [16].

5. CONCLUSION

The elevated values of urea, creatinine, sodium, potassium in the serum,plasma glucose and urine protein precludes them to be useful for consideration as consistent predictive indicator(s) for preeclampsia or pregnancy related hypertension. Furthermore the elevated values for plasma glucose and urine protein could be used to differentiate between moderate and sever preeclampsia. Therefore it was recommended that all pregnant women should be screened for preeclampsia at the first prenatal visit and periodically throughout the remainder of the pregnancy.

CONSENT

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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