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# Association of chronic medical conditions with preterm labor

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**Original Article**

## Abstract

**BACKGROUND:** Prematurity is the most common cause of neonatal death and according to Millennium Development Goal (MDG), two-thirds of all under-five deaths should be reduced by 2015. Therefore, this study examined factors related to preterm birth in Sanandaj, Iran in 2012.

**METHODS:** This case-control study has been conducted on 600 pregnant women; cases were 200 women with preterm labor and controls were 400 women with term labor, in Be'sat Hospital, Sanandaj, Iran, in 2012. Results were analyzed by Chi-square, Mann-Whitney U and logistic regression tests.

**RESULTS:** In univariate analysis, overt diabetes ($P = 0.030$), chronic hypertension ($P < 0.001$), preeclampsia and eclampsia ($P < 0.001$), had significant correlations with preterm labor. However, multivariate analysis results showed that factors like preeclampsia and eclampsia ($P < 0.001$) and chronic hypertension ($P = 0.030$) had significant correlation with the incidence of premature birth. In univariate and multivariate analysis, anemia ($P = 0.340$) had not any association with the preterm labor.

**CONCLUSION:** The results of this study showed some chronic maternal conditions such as chronic hypertension and diabetes mellitus, which are important pre-existing medical disorder complicating pregnancy and control of blood pressure and blood sugar before pregnancy, and have an important effect in decreased of preterm labor and complications. But others such as mother's anemia were not responsible for the prematurity.

**KEYWORDS:** Prematurity, Diabetes, High Risk Mothers, Hypertension

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## Introduction

Premature birth is defined as delivery before 37 completed weeks of gestation and after congenital anomalies; it is the most common cause of death and disease in newborns.[1] It is one of the big challenges in the care of pregnant women during prenatal care.[2] Each year, 13 million premature babies are born in the world, of which 3.1 million of them die in the neonatal period. Statistics shows the rate of premature birth in the United States increased by 21% compared to 1990;[3] although the incidence of preterm birth remains at 12% higher than in many developed countries.[4] Premature births are the cause of 27% of annual infant mortality worldwide, 70% of perinatal mortality in developing countries, and 50% of neurological disorders.[5]

Although in most cases the reason for preterm labor cannot be found, the known risk factors are exclusive of labor itself. These factors include demographical factors, obstetric history, cervical and uterine factors, multigravity, bleeding and chronic diseases. One of the most common and avoidable factors is maternal chronic medical conditions including pre-pregnancy diabetes mellitus, chronic hypertension (essential or pregnancy induced), untreated anemia and urinary tract infections (UTI), which are

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responsible for large number of preterm labor.[6-15]

In pregnancy, chronic hypertension is associated with increased incidences of placental abruption, acute renal failure, cardiac decompensation, cerebral accidents and preterm labor in mothers.[7] Diabetes also increases the risk of preterm delivery not only as an independent factor, but also through its complications, including increased risk of infection, increased abnormal amniotic fluid (polyhydroamnious); severe hypertension and worsening of diabetic nephropathy could impose delivery to mother and fetus.[7,8]

In Kurdistan province, the most common causes related to neonatal mortality were prematurity that accounts for 42.5% of all perinatal deaths.[16] Despite high incidence of preterm labor as a major health problem in this province, unfortunately, no study has ever been performed on the role of mothers underlying medical condition and preterm labor. So this study has been designed and implemented to investigate the role of chronic diseases such as diabetes mellitus, chronic hypertension, anemia and UTI before pregnancy on the incidence of preterm birth after excluding confounding factors (maternal age, preeclampsia and eclampsia, bleeding etc.).

## Materials and Methods

This case-control study has been conducted on 600 pregnant mothers in Be'sat Hospital, Sanandaj, Iran, in 2012. Cases included mothers who were delivered before 37 weeks and after 20 weeks of gestational age and preterm labor was approved by their medical care records and ultrasounds. The control group was mothers delivered between 37 to 42 weeks of pregnancy.

Sample size of 196 cases were calculated, considering type I error 5%, power 85%, acceptable Odd Ratio (OR = 2) and control group prevalence of risk factors about 20%. To increase the accuracy of the test, for each case two controls were selected.

For data collection, a trained midwife checked mothers in the postpartum ward (where mothers are transferred to shortly after childbirth) as well as the medical records of the newborns (including ultrasound and medical reports). Then in case of encountering preterm infant, those cases were enrolled in the study. Thereafter, two other newborns, closest in time to the birth of the preterm, were selected as the controls. Furthermore, maternal deaths during childbirth were recorded each day for identifying bias in the study.

Hypertension is defined as blood pressure ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic (preferably confirmed by two readings, 4 to 6 hours separately). Diabetes mellitus is defined as fasting blood sugar (FBS) above 126 in two separate measurements or random FBS more than 200 with classic symptoms of hyperglycemia. Anemia is defined as hemoglobin less than 12 mg/dl and hematocrit < 36% in complete blood count (CBC) done in first prenatal visit.

Data were analyzed using SPSS for Windows (version 11.5, SPSS, Inc., Chicago, IL, USA). Then quantitative and qualitative data were compared between the two groups using t-test, Mann-Whitney U-test and chi-square test, respectively. At this stage, variables with P value less than 0.05 were entered into the logistic regression model. After preparing the model, variables with high P value were excluded from the model which resulted in a model that could explain maximum likelihood estimation of variances.

## Results

Out of a total 600 cases, 10 infants died, 9 were preterm and 1 had cardiac anomalies. Mann-Whitney U test showed no statistically significant difference between the two groups.

Given the following string variables; preterm labor in history of previous premature babies (OR = 4.8; P < 0.001), number of dead children (OR = 2.58; P = 0.011), olygohydramnious (OR = 3.3; P < 0.001), premature rupture of membranes (OR = 3.5; P < 0.001); double and multiple pregnancies (OR = 10.8; P < 0.001), overt diabetes mellitus (OR = 3.5; P = 0.030), chronic hypertension (OR = 2.6; P < 0.001),

preeclampsia and eclampsia (OR = 3.5; P < 0.001), infertility (OR = 3.9; P < 0.001) and cervical insufficiency (OR = 7.3; P < 0.001) in univariate analysis showed statistically significant association with preterm labor. However, mother's age, occupation and education, showed no statistically significant association with the preterm labor (Table 1).

Based on multivariate analysis, amniotic fluid reduction (OR = 3.7; P < 0.001), double and multiple pregnancies (OR = 12.1; P < 0.001), chronic hypertension (OR = 2.04; P = 0.030),

**Table 1. Comparison of maternal variables between case and control groups**

| Variable | Status | Groups [n (%)] | | Total [n (%)] | OR (CI 95%) | P |
|---|---|---|---|---|---|---|
| | | Preterm | Term | | | |
| Previous delivery | NVD | 77 (34.1) | 149 (65.9) | 266 (100) | 0.665 (0.411-1.077) | 0.096 |
| | C/S | 33 (25.6) | 96 (74.4) | 129 (100) | | |
| Previous child death | No | 184 (32.2) | 387 (67.8) | 571 (100) | 2.58 (1.22-5.49) | 0.011 |
| | Yes | 16 (55.2) | 13 (44.8) | 29 (100) | | |
| Amniotic fluid status | Normal | 152 (29.3) | 366 (70.7) | 518 (100) | 3.325 (2.059-5.380) | < 0.001 |
| | Abnormal | 47 (58.0) | 34 (42.0) | 81 (100) | | |
| Premature rupture of membranes (PROM) | No | 97 (23.9) | 309 (76.1) | 406 (100) | 3.571 (2.483-5.134) | < 0.001 |
| | Yes | 102 (52.8) | 91 (47.2) | 193 (100) | | |
| Twin | Single | 146 (27.4) | 387 (72.6) | 533 (100) | 10.807 (5.822-20.408) | < 0.001 |
| | Twin and more | 53 (80.3) | 13 (19.7) | 66 (100) | | |
| Infant gender | Girl | 75 (29.8) | 177 (70.2) | 252 (100) | 1.329 (0.938-1.882) | 0.109 |
| | Boy | 125 (36.0) | 222 (64.0) | 347 (100) | | |
| History of prematurity | No | 182 (31.7) | 392 (68.3) | 574 (100) | 4.846 (2.069-11.352) | < 0.001 |
| | Yes | 18 (69.2) | 8 (30.8) | 26 (100) | | |
| History of overt diabetes mellitus | No | 193 (32.8) | 395 (67.2) | 588 (100) | 3.582 (1.036-12.383) | 0.032 |
| | Yes | 7 (63.7) | 4 (36.4) | 11 (100) | | |
| Gestational diabetes mellitus (GDM) | No | 166 (33.0) | 337 (67.0) | 503 (100) | 1.096 (0.694-1.730) | 0.695 |
| | Yes | 34 (35.1) | 63 (64.9) | 97 (100) | | |
| Chronic hypertension | No | 156 (30.2) | 361 (69.8) | 517 (100) | 2.611 (1.631-4.176) | < 0.001 |
| | Yes | 44 (53.0) | 39 (47) | 83 (100) | | |
| Preeclampsia and eclampsia | No | 166 (30.5) | 378 (69.5) | 544 (100) | 3.519 (1.997-6.201) | < 0.001 |
| | Yes | 34 (60.7) | 22 (39.3) | 56 (100) | | |
| Infertility | No | 175 (31.2) | 386 (68.8) | 561 (100) | 3.939 (1.999-7.761) | < 0.001 |
| | Yes | 25 (64.1) | 14 (35.9) | 39 (100) | | |
| Urinary tract infection (UTI) | No | 169 (34.0) | 328 (66.0) | 497 (100) | 0.847 (0.534-1.344) | 0.481 |
| | Yes | 31 (30.4) | 71 (69.6) | 102 (100) | | |
| Anemia | No | 140 (32.3) | 294 (67.7) | 519 (100) | 1.200 (0.824-1.747) | 0.341 |
| | Yes | 60 (36.4) | 105 (63.6) | 80 (100) | | |
| Place of residence | City | 115 (31.2) | 254 (68.8) | 369 (100) | 1.280 (0.904-1.811) | 0.164 |
| | Village | 84 (36.7) | 145 (63.3) | 229 (100) | | |
| Mother's job | Housekeeper | 194 (33.3) | 388 (66.7) | 582 (100) | 0.833 (0.289-2.399) | 0.735 |
| | Employed | 5 (29.4) | 12 (70.6) | 17 (100) | | |
| History of cervical insufficiency | No | 174 (30.8) | 391 (69.2) | 589 (100) | 7.303 (3.241-16.455) | < 0.001 |
| | Yes | 26 (76.5) | 8 (23.5) | 34 (100) | | |
| Age groups | 18-35 years old | 175 (33.8) | 343 (66.2) | 518 (100) | 1.960 (0.677-5.676) | 0.215 |
| | Less than 18 years old | 7 (50.0) | 7 (50.0) | 14 (100) | | |

OR: Odd Ratio; CI: Confidence interval; NVD: Normal vaginal delivery; C/S: Cesarean section

previous history of preterm labor (OR = 3.8; P = 0.011) were all significantly associated with the incidence of preterm labor. However, in multivariate analysis, pre-pregnancy diabetes mellitus (P = 0.230), was not associated with prematurity (Table 2).

In both univariate and multivariate analyses, anemia (P = 0.340) and UTI (P = 0.480) were not associated with prematurity (Table 1).

## Discussion

In univariate analysis, history of previous premature babies, number of dead children, premature rupture of membranes (PROM), olygohydramnious, double and multiple pregnancies, overt diabetes mellitus, chronic hypertension, preeclampsia and eclampsia, infertility and cervical insufficiency had statistically significant relation with the occurrence of preterm labor. But mother's age, occupation, anemia and urinary tract infections had no statistically significant relation with the occurrence of preterm labor. However, after logistic regression analysis, abnormal amniotic fluid, PROM, double and multiple pregnancy, hypertension, preeclampsia and eclampsia, maternal age of over 35 years, and previous preterm labor were significantly associated with the incidence of preterm labor. In univariate analysis, variables that were statistically significant and were associated with prematurity could be considered as risk factors for screening high risk women who should receive more attention during pregnancy. However, these factors could be correlated; hence some of them were not significant in multivariate analysis.

In univariate analysis, data showed a statistically significant association between diabetes mellitus and prematurity (but not gestational diabetes mellitus). But in multivariate analysis, there was no association between the pre-pregnancy diabetes mellitus which was in accordance with some other studies. It might be related to the small sample size in our study or it may be neutralized with others variable (such as age, hypertension, etc) in multivariate analysis. On the other hands, one of the important complications of diabetes is chronic hypertension, so diabetes can be affected by the hypertension. However, based on gynecology and obstetrics clinical references and most studies, as an independent risk factor, diabetes can directly or indirectly (e.g. by increasing risk of infection, and polyhydroamnious, hypertensive disorders and severe diabetic nephropathy) trigger a preterm delivery.[8,13,17] In Sibai et al., women with diabetes mellitus had significantly higher rates of both indicated preterm delivery and spontaneous preterm delivery did women in the control group.[13]

In this study, chronic hypertension had a significant association with preterm labor. In multivariate analysis, preeclampsia and

**Table 2. Multivariate analysis of factors influencing prematurity**

| Variables | B | Standard error | Wald | P | Adjusted OR | 95% CI for OR | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower | Upper |
| Amniotic Fluid Reduction | 1.316 | 0.272 | 23.370 | < 0.001* | 3.729 | 2.187 | 6.358 |
| Twin | 2.494 | 0.362 | 47.576 | < 0.001* | 12.107 | 5.961 | 24.592 |
| Sex (male) | 0.222 | 0.204 | 1.184 | 0.277 | 1.248 | 0.837 | 1.860 |
| Previous preterm labor | 1.353 | 0.533 | 6.435 | 0.011 | 3.867 | 1.360 | 10.996 |
| Overt diabetes mellitus | 1.032 | 0.870 | 1.407 | 0.236 | 2.807 | 0.510 | 15.445 |
| Hypertension | 0.714 | 0.333 | 4.592 | 0.032* | 2.041 | 1.063 | 3.921 |
| Preeclampsia and eclampsia | 0.962 | 0.395 | 5.940 | 0.015* | 2.618 | 1.207 | 5.676 |
| Cervical insufficiency | 0.529 | 0.471 | 1.265 | 0.261 | 1.698 | 0.675 | 4.271 |
| Age group | - | - | 8.067 | 0.018* | - | - | - |
| < 18 years | 0.766 | 0.637 | 1.446 | 0.229 | 2.151 | 0.617 | 7.497 |
| > 35 years | -0.961 | 0.379 | 6.428 | 0.011* | 0.383 | 0.182 | 0.804 |

* Statistically significant; OR: Odd Ratio; CI: Confidence interval

eclampsia also had a significant association with preterm labor. According to many studies, hypertensive disorders in pregnancy include four categories, uncontrolled chronic hypertension, preeclampsia superimposed on chronic hypertension, gestational hypertension and preeclampsia and eclampsia. Therefore, it seems that chronic hypertension, itself, and in addition through superimposing preeclampsia and other complications can investigate the pregnancy's outcome.[2,18] In Sibai et al., mothers with chronic hypertension compared with control group, had higher rates of indicated preterm delivery.[13] In Xiong's study,[19] gestation was 0.6 week shorter in women with severe preeclampsia than in normotensive women. But the risk of preterm labor was not increased with any classification of pregnancy-induced hypertension. Although most studies confirmed a significant association between preeclampsia with preterm birth,[17,20,21] our objective was to remove the effect of preeclampsia and eclampsia and examine the role of chronic hypertension.

In our study, there was no association between mother's anemia before pregnancy and prematurity. Perhaps, the development of prenatal care and giving ferrous sulfate supplementation in early pregnancy reduced the rate of anemia in all the pregnant women. The result of Kang and Lin's study[22] was also similar to us. But in Bora et al.,[23] maternal anemia was increased preterm labor and each 10 µg/l decrease in maternal hemoglobin was associated with 0.18 week decrease in gestational length.

In this study, the most cause of hospitalization of mothers was urinary tract infections and a high percentage of mothers suffered from vaginal discharge and dysuria, but genitourinary infections were not associated with preterm labor. In the study of Ebrahimi,[24] UTI was more common in preterm labor but without any significant association with preterm labor. In some others, women with UTI especially acute pyelonephritis had threatened preterm labor.[25-27]

## Conclusion

The results of this study showed that some chronic maternal conditions such as chronic hypertension and diabetes mellitus are important pre-existing medical disorder complicating pregnancy and control of blood pressure and blood sugar before pregnancy have an important impact on declining preterm labor and complications. But others such as mother's anemia were not responsible for the prematurity.

## Conflict of Interests

Authors have no conflict of interests.

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## References

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005; 365(9455): 217-23.
2. Leeman L, Fontaine P. Hypertensive disorders of pregnancy. Am Fam Physician 2008; 78(1): 93-100.
3. Ashton DM, Lawrence HC, Adams NL, Fleischman AR. Surgeon General's Conference on the Prevention of Preterm Birth. Obstet Gynecol. 2009; 113(4): 925-30.
4. Chandra Dey A, Mannan A, Saha L, Hossain I, Shahidullah M. Magnitude of Problems of Prematurity-National and Global Perspective: A Review. Bangladesh J Child Health 2012; 36 (3): 146-52.
5. Sepanlou SG, Kamangar F, Poustchi H, Malekzadeh R. Reducing the burden of chronic diseases: a neglected agenda in Iranian health care system, requiring a plan for action. Arch Iran Med 2010; 13(4): 340-50.
6. Haghdoost AA, Mirzazadeh A. Familial Aggregation of Coronary Heart Disease Risk Factors in Kerman Province. Iran J Epidemiol 2006; 1(3): 7-12.
7. Gilbert WM, Young AL, Danielsen B. Pregnancy outcomes in women with chronic hypertension: a

population-based study. J Reprod Med 2007; 52(11): 1046-51.
8. Reece A, Homko CJ. Diabets mellitus and pregnancy. In: Gibbs RS, Editor. Danforth's Obstetrics and Gynecology. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008. p. 246-56.
9. Watchko JF. Seminars in fetal and neonatal medicine "continuing controversies in perinatal jaundice". Semin Fetal Neonatal Med 2010; 15(3): 121.
10. Azizi F, Janghorbani M, Hatami H, Azizi T, Agha Abbasloo M. Nourologic system of disease. In: Azizi F, Janghorbani M, Hatami H, Azizi T, Agha Abbasloo M, Editors. Epidemiology and control of common disease in Iran. Tehran, Iran: Khosravi Publication; 2010. p. 195-202. [In Persian].
11. Khader Y, Al-shishani L, Obeidat B, Khassawneh M, Burgan S, Amarin ZO, et al. Maternal periodontal status and preterm low birth weight delivery: a case-control study. Arch Gynecol Obstet 2009; 279(2): 165-9.
12. Boots AB, Sanchez-Ramos L, Bowers DM, Kaunitz AM, Zamora J, Schlattmann P. The short-term prediction of preterm birth: a systematic review and diagnostic metaanalysis. Am J Obstet Gynecol 2014; 210(1): 54.
13. Sibai BM, Caritis SN, Hauth JC, MacPherson C, VanDorsten JP, Klebanoff M, et al. Preterm delivery in women with pregestational diabetes mellitus or chronic hypertension relative to women with uncomplicated pregnancies. The National institute of Child health and Human Development Maternal- Fetal Medicine Units Network. Am J Obstet Gynecol 2000; 183(6): 1520-4.
14. Kramer MS, Goulet L, Lydon J, Seguin L, McNamara H, Dassa C, et al. Socio-economic disparities in preterm birth: causal pathways and mechanisms. Paediatr Perinat Epidemiol 2001; 15(Suppl 2): 104-23.
15. Mercer BM, Goldenberg RL, Das A, Moawad AH, Iams JD, Meis PJ, et al. The preterm prediction study: a clinical risk assessment system. Am J Obstet Gynecol 1996; 174(6): 1885-93.
16. Esmailnasab N, Afkhamzadeh AB, Biglari F. Study of epidemiologic survey of perinatal mortality in Kurdistan [Thesis]. Sanandaj, Iran: School of Medicine, Kurdistan University of Medical Science; 2011. [In Persian].
17. Wagner SJ, Barac S, Garovic VD. Hypertensive pregnancy disorders: current concepts. J Clin Hypertens (Greenwich) 2007; 9(7): 560-6.
18. Lindheimer MD, Conrad KP, Karumanchi SA. Renal Physiology and Disease in Pregnancy. In: Alpern RJ, Hebert SC, Editors. Seldin and Giebisch's The Kidney: Physiology & Pathophysiology. 4th ed. New York, NY: Academic Press; 2007. p. 2339-98.
19. Xiong X, Mayes D, Demianczuk N, Olson DM, Davidge ST, Newburn-Cook C, et al. Impact of pregnancy-induced hypertension on fetal growth. Am J Obstet Gynecol 1999; 180(1 Pt 1): 207-13.
20. Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC, et al. Factors associated with preterm birth in Cardiff, Wales. I. Univariable and multivariable analysis. Am J Obstet Gynecol 1995; 173(2): 590-6.
21. Mohsenzadeh A, Saket S, Karimi A. Prevalence of preterm neonates and risk factors. Iran J neonatal 2011; 2(2): 38-42.
22. Kang JH, Lin HC. Stroke during pregnancy: no increased risk of preterm delivery and low birth weight, a nationwide case-controlled study. J Neurol Neurosurg Psychiatry 2010; 81(11): 1211-4.
23. Bora R, Sable C, Wolfson J, Boro K, Rao R. Prevalence of anemia in pregnant women and its effect on neonatal outcomes in Northeast India. J Matern Fetal Neonatal Med 2013.
24. Ebrahimi S, Haghbin S, Poor Mahmoodi A. Incidence and etiologic factors of prematurity. Armaghane-danesh 2000; 5(19-20): 41-35. [In Persian].
25. Afrakhteh M, Ebrahimi S, Valaei N. Prevalence of preterm delivery and its related factors in females referring to Shohada Tajrish Hospital, 1995-99. Pejouhandeh 2003; 7(4): 341-4. [In Persian].
26. Al-Dabbagh SA, Al-Taee WY. Risk factors for pre-term birth in Iraq: a case-control study. BMC Pregnancy Childbirth 2006; 6: 13.
27. Jolley JA, Kim S, Wing DA. Acute pyelonephritis and associated complications during pregnancy in 2006 in US hospitals. J Matern Fetal Neonatal Med 2012; 25(12): 2494-8.