

## Investigating of the demographic, socioeconomic, and obstetric risk factors of term intrauterine stillbirth cases

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### Abstract

**Objective:** To establish the prevalence, etiology, demographic, socioeconomic, and obstetric risks factors of intrauterine fetal deaths among term pregnancies with no risk factors. Our study is the first to investigate term stillbirth risk factors in such a large population.

**Material and Methods:** A total of 96 cases of stillbirth between 37th and 42nd weeks with no risk factors out of 90,557 births conducted in 2011-2015 were investigated retrospectively. Eighty patients that had stillbirth in our clinic were chosen as the study cases and 80 others that had risk-free live birth at the weeks of 37-42 chosen randomly accepted as the control group. Variables such as age of mothers, gravidas, parities, level of education of mothers, time since the previous pregnancy, BMIs, weight gained during pregnancy, gestational week, birth weights of infants, systolic and diastolic blood pressures, hemoglobin values, blood glucose levels, white blood cell counts, smoking history, follow-ups at the hospital, gender of babies, and seasonal distribution of stillbirths were evaluated.

**Results:** The stillbirth rate was found as 14 per million and stillbirth in risk-free population at 37-42 weeks was 1.05 per mill. BMI, hemoglobin levels, and systolic blood pressures of mothers were significantly higher in stillbirths. Any statistically significant difference in mean maternal age, gravida/parity, education level, weight gained during pregnancy, smoking and fetal gender distribution was not established between the groups

**Conclusion:** Term stillbirths in the risk-free group may be correlated with advanced gestational week, increased BMI, systolic blood pressure, and hemoglobin levels of the mother also insufficient antenatal follow-up.

**Keywords:** stillbirth, antenatal follow-up, intrauterine exitus, risk factors

### Introduction

Worldwide stillbirth rate was shown as 18.4 per million. While this rate and its causes may manifest differences according to countries and even to various regions in a given country, it is observed more in developing countries compared to developed countries (1). Stillbirth rates were established as 0.2% in developed countries, 0.7% in developing countries, and as 2% in South Africa and in certain countries in Asia (2).

Worldwide stillbirth rate was found as 18.4 per mill in 2015, and while the said rate appears to be promising when compared with 18.9 in 2009 and 19.4 in 2000, there is still a need for enlightenment and precautions (3). According to the WHO data, there were 2.6 million stillbirth cases in 2015, and 98% of these cases have been observed in developing or backward countries (3).

ENAP (Every Newborn Action Plan) pulls the 2030 stillbirth rate target down to 12 per mill. In Turkey, stillbirth rate is 9 per mill according to TNS 2013 data.

Such causes of fetal death as syphilis, RH isoimmunisation, preeclampsia-hypertension, and diabetes complicate pregnancy gradually less thanks to antenatal care and treatment. However, intrauterine infections, lethal malformations, chromosomal anomalies, fetal growth retardation, and ablation placentae still cause fetal death in numerous pregnancies (4).

While the determination of causes found in the etiology of stillbirths has shown an increase, one of the factors that would be the cause of death may not always be established in intrauterine deaths (5).

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Rate of stillbirth with no known cause among all still births ranges is between 12% and 50% in the literature (6-9).

The aim of this study is to establish the prevalence, etiology, demographic, socioeconomic, and obstetric risks factors of intrauterine fetal deaths among pregnancies between 37th and 42nd weeks with no risk factors, to determine preventable risk factors, hence, to foresee the precautions necessary to be taken and to increase the healthy mother and infant rate. Our study is the first to investigate term stillbirth risk factors in such a large population.

## Material and Methods

A total of 96 cases of stillbirth between 37th and 42nd weeks with no risk factors out of 90,557 births conducted in Zekai Tahir Burak Gynaecology and Obstetrics Training and Research Hospital in 2011-2015 were investigated retrospectively. Patients with systemic diseases, obstetric complications, and previous uterine surgery were excluded from the study. Of these cases, 16 were excluded from the study due to insufficient, but 80 were included in the study.

All the information on cases were collected from computer records, record books, and patient files. Eighty patients that had stillbirth in our clinic were chosen as the study cases and 80 others that had risk-free live birth at the weeks of 37-42 and chosen randomly were accepted as the control group. All the cases that had absent fetal cardiac activity determined by ultrasonography had been established by the records.

In selecting the cases, attention was paid in cases being in the age range of 17-43, last menstrual date of gestational week and above 37 weeks based on ultrasonography, and the absence of fetal cardiac activity (by USG), cases that had chronic diseases (such as diabetes, hypertension, goitre, asthma), thrombophilia, uterine anomaly and previous uterine operations, that had embryo reduction, and cases with missing or insufficient birth information were excluded from the study.

Variables such as age of mothers in both groups, gravidas, parities, level of education of mothers, time since the previous pregnancy, BMIs, weight gained during pregnancy, gestational week based on the last menstrual date and ultrasound, birth weights of infants, systolic and diastolic blood pressures, hemoglobin values, blood glucose levels, white blood cell counts, smoking history, follow-ups at the hospital, gender of babies, and seasonal distribution of stillbirths were evaluated. While assessing the data obtained from the study, SPSS for Windows 22.0 software was used for statistical analyses. While analyzing the study data, mean, median, and standard deviation that are descriptive statistical methods were utilized. Compatibility of study group to normal distribution was carried out by using Shapiro Wilks Normalization Test. As data was not compatible with normal distribution, Mann-Whitney U test was utilized for the comparison of parameters between the groups. Chi square test was used for the comparison of qualitative data. The results were evaluated in 95% confidence interval and significance was assessed at  $p < 0.05$  level.

## Results

In our study, the stillbirth rate was found as 14 per million (/106) and stillbirth in risk-free population at 37-42 weeks was 1.05 per mill. Mean gestational week of the stillbirth group was  $39.07 \pm 1.34$ , and this was established as significantly high compared to live births ( $p: 0.005$ ). Mean weight of stillborn babies in our study (3087gr) was established as statistically significantly low compared to babies in the control group (3311gr) ( $p < 0.05$ ). Antenatal polyclinic follow-up count in the stillbirth group was lower compared to the control group so as to manifest a statistical significance ( $p < 0.05$ ). BMI, hemoglobin levels, and systolic blood pressures, of mothers that had stillbirth were statistically significantly higher compared to the control group ( $p < 0.05$ ). Any statistically significant difference in mean maternal age, gravida and parity counts, level of education, weight gained during pregnancy, smoking history, and fetal gender distribution was not established between the groups in our study ( $p > 0.05$ ).

**Table 1:** Comparison of Data Based on the Groups (Mean $\pm$ SD)

	Case (n=80)	Control (n=80)	P
<b>Gestational Week</b>	39.07 $\pm$ 1.34	38.51 $\pm$ 1.23	<b>0.005</b>
<b>Age</b>	28.37 $\pm$ 6.47	27.37 $\pm$ 5.78	0.38
<b>Gravida</b>	2.45 $\pm$ 1.69	2.23 $\pm$ 1.13	0.99
<b>Parity</b>	1.12 $\pm$ 1.39	0.96 $\pm$ 0.89	0.78
<b>Time between pregnancies</b>	3.50 $\pm$ 4.16	3.11 $\pm$ 3.49	0.96
<b>BMI</b>	30.90 $\pm$ 4.81	29.19 $\pm$ 4.14	<b>0.02</b>
<b>Systolic Blood Pressure</b>	112.87 $\pm$ 10.21	108.25 $\pm$ 8.96	<b>0.006</b>
<b>Diastolic Blood Pressure</b>	69.50 $\pm$ 8.55	68.75 $\pm$ 7.18	0.55
<b>Infant Birth Weight</b>	3087.50 $\pm$ 431.84	3311.87 $\pm$ 407.94	<b>0.000</b>
<b>Blood Glucose</b>	96.82 $\pm$ 34.27	88.04 $\pm$ 21.00	0.09
<b>White Blood Cell</b>	11636.87 $\pm$ 3060.18	15578.75 $\pm$ 23518.58	0.38
<b>Hemoglobin</b>	14.78 $\pm$ 16.86	11.72 $\pm$ 1.20	<b>0.007</b>
<b>Weight Gained during Pregnancy</b>	12.58 $\pm$ 4.28	11.15 $\pm$ 3.98	0.88

*Data were given as mean  $\pm$  Standard Deviation.  $P < 0.05$  was accepted as statistically significant. Mann-Whitney U Test.*

Table 2. Distribution of Properties Between the Study Groups

Groups		Case (n=80)	Control (n=80)	p
<b>Gestational Week</b>	37	12 (15)	17 (21.3)	<b>0.005</b>
	38	16 (20)	29 (36.3)	
	39	19 (23.8)	18 (22.5)	
	40	23 (28.8)	9 (11.3)	
	41	6 (8.8)	6 (7.5)	
	42	1 (3.8)	1 (1.3)	
<b>BMI</b>	18.5≤	0	0	<b>0.02</b>
	18.6-24.9	9 (11.3)	17 (21.3)	
	25-29.9	25 (31.3)	29 (36.3)	
	≥30	46 (57.5)	34 (42.5)	
<b>Education Level</b>	Illiterate	10 (12.5)	4 (5)	0.23
	Elementary School	27 (33.8)	26 (32.5)	
	Middle School	21 (26.3)	19 (23.8)	
	High School	13 (16.3)	23 (28.8)	
	Higher Education	9 (11.3)	8 (10)	
<b>Follow-up Status</b>	Yes	26	50	<b>0.000</b>
	No	54	30	
<b>Smoking</b>	Yes	3	6	0.49
	No	77	74	
<b>Sex</b>	Female	31	38	0,29
	Male	49	42	

Date were given as n (%). P<0.05 was accepted as statistically significant.

## Discussion

Total number of births in our clinic in five years between 2011 and 2015 was 90,557 as obtained from the department of statistics in our hospital. Between these dates, stillbirths occurring at 28th week and above were 1,326. Of these cases, stillbirths that occurred in the group containing cases at 37-42 weeks bearing no risk factors, that were being followed up in antenatal polyclinic or that were referred to us by outside centres upon receiving diagnosis intrauterine fetal death were 96.

Global stillbirth rate is about 14 per million. Our stillbirth rate between the weeks of 37 and 42 in pregnancies without any risk factors was found as 1.05 per mill.

We established in our study that term stillbirths in the risk-free group may have a correlation with advanced gestational week, increased body-mass index, increased systolic blood pressure, and increased hemoglobin levels of the mother. In addition, we also established the need to count insufficient antenatal follow-up among the factors increasing the stillbirth risk.

Many studies show the advanced maternal age as an independent risk factor (10). Intrauterine fetal loss significantly increases especially above the maternal age of 35. Ling Huang et al. established that the stillbirth rate statistically significantly increases as the maternal age advances. An increase by 1.26-1.92 times was found in women aged 35 and above compared to women below the age of 35 (11). In our study, a statistically significant difference was not established between the mean ages of case and control groups (p>0.05).

We believe the determining factor of this are our scans in certain week intervals and increased number of exclusion criteria. In addition, the fact that age distribution was not equal may be counted as one of the reasons.

Multiparity is also deemed a risk factor due to it impacting the physiology of the mother in stillbirth cases. In addition, nulliparity is an independent risk factor when analyzed on its own or together with other risk factors. In a study carried out by Adrienne Gordon et al., while a significant difference was not found between the multipara and nullipara, a significant risk increase was established in nulliparous women aged above 40 as subgroup. (12). In our study, too, a statistically significant difference was not found between the gravidas of case and control group members (p>0.05). There are studies in literature that reached conclusions similar to our study (13).

Socioeconomic status was believed to have had an impact on the number of follow-ups conducted at the hospital and the feeding level of the mother, and similarly, it was accepted as a preventable risk factor due to the effect of the education level of the mother on the awareness and its contribution to figure out the pregnancy risk factors at early stages and prevent them. According to literature, while low levels of education pose 1.5 times adjusted relative risk compared to high levels of education, medium levels of education were established as having 1.4 times adjusted relative risk (14). Due to the fact that, in our hospital, patients with low levels of income and low levels of education receive treatment, a difference was not observed between the groups in terms of the levels of education.

However, a statistically significant difference was established between the case and control groups in terms of follow-up conditions ( $p < 0.05$ ). Number of unfollowed cases in the case groups was found as higher compared to the control group, which manifests similar characteristics with the literature.

Without a doubt, one of the most discussed issues in recent years among stillbirth risk factors is BMI. According to the study by Addo et al., obese patients were observed to be shorter, older, and gained more weight during pregnancy, and as a result, the stillbirth rate was found significantly higher (OR=3.12 %95 CI :1.42-7.57)(15). Whiteman et al. also established that stillbirth risk increases parallel to the rise in BMI (16). In our study, too, a statistically significant difference was found between BMIs of case and control group patients ( $p < 0.05$ ). Based on our study, rise in the BMI increased the stillbirth risk. In this study, a statistically significant difference was not established between the average weight gained during pregnancy in both groups ( $p > 0.05$ ). As a result, high BMI levels found in the case group suggests that the case group was pre-gestational overweight and that this finding show similarities in numerous studies in literature (16).

It was believed that male fetal gender possessed higher risk in terms of stillbirth, and the reason for this was suggested as the physiological differences between genders and their effects on the mother's physiology. It was also argued that the differences between male and female placenta could be a factor in this. There are contradicting publications on male gender and increased fetal death risk (17, 18). In our study, a statistically significant difference was not found between the groups in terms of fetal gender ( $p > 0.05$ ).

Studies appear to support that low birth weight increases stillbirth risk (19). In their study, Cnattingius et al. concluded that SGA (Small for Gestational Age) babies increased the stillbirth risk independently from other factors (20). In our study, too, birth weights of the case group were found as statistically significantly lower compared to the control group. It is important to take into consideration the low fetal weight determined during pregnancy follow-ups.

Smoking has been thoroughly investigated in terms of causing IUGR (Intrauterine Fetal Growth Restriction) and is among the agents whose effectiveness was manifested through dose-response curves (21). Smoking increases the stillbirth risk both on its own and indirectly thanks to other results caused by smoking.

(22). According to a meta-analysis in literature, smoking throughout the pregnancy increases stillbirth risk by 47% (23). Similarly, based on the data by the National Center for Health Statistics in the US, smoking increases relative stillbirth rate by 1.2-1.8 times (24). In our study, a statistically significant difference was not found between case and control groups in terms of smoking ( $p > 0.05$ ).

In literature, while anaemia is believed to have a correlations predominantly with preterm labour and SGA, there exist studies that show that hemoglobin levels above 13.9 are related with increased maternal morbidity and SGA (25, 26). In similar fashion, it was found that high

hemoglobin levels measured at the first visit have correlations with negative pregnancy results and stillbirth risk (27). In our study, too, the hemoglobin levels of the case group were found as higher compared to the control group ( $p < 0.05$ ).

Seyom et al. found the stillbirth rate in patients with hypertension as 10.1% (28). In our study, too, systolic blood pressures of the case group were found as higher compared to the control group while complying with the literature.

Correlation between gestational week and stillbirth is still among the leading discussion topics. According to their study, Nicholson et al. established that there occurred an increase in stillbirth incidence in 7 years especially since the implementation of 39-week rule (29). They involuntarily commenced a discussion that the 39-week rule may be damaging. In our study, mean gestational week of the case group was  $39.07 \pm 1.34$  and mean gestational week of the control group was  $38.51 \pm 1.23$ , and there was statistically significant difference ( $p < 0.05$ ). Accordingly, it should be borne in mind that gestational week poses a risk in the group with no risk factors in terms of stillbirth. It is necessary to be on alert bearing in mind stillbirths by assessing the patients in more detail in the coming weeks.

## Conclusion

Consequently, we established in our study that term stillbirths in the risk-free group may be correlated with advanced gestational week, increased body-mass index, increased systolic blood pressure, and increased hemoglobin levels of the mother. In addition, we also showed that the insufficient antenatal follow-up should be counted among the factors increasing the stillbirth risk.

Results of this study may contribute to gravitating towards primary preventive healthcare programmes that specifically contain antenatal care. Stillbirth rates may be decreased by expanding the antenatal care services in primary and secondary centres, detecting high-risk pregnancies at earlier gestational stages, and taking necessary medical precautions.

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## References

1. Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, Hogan D, Shiekh S, Qureshi ZU, You D, Lawn JE. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. *The Lancet Global Health*. 2016 Feb 1;4(2):e98-108.
2. Stanton C, Lawn JE, Rahman H, Wilczynska-Ketende K, Hill K. Stillbirth rates: delivering estimates in 190 countries. *The Lancet*. 2006 May 6;367(9521):1487-94.



3. Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, Flenady V, Frøen JF, Qureshi ZU, Calderwood C, Shiekh S. Stillbirths: rates, risk factors, and acceleration towards 2030. *The Lancet*. 2016 Feb 6;387(10018):587-603.
4. Sims MA, Collins KA. Fetal death: a 10-year retrospective study. *The American journal of forensic medicine and pathology*. 2001 Sep 1;22(3):261-5.
5. Cunningham FG, MacDonald PC, Gant NF, Leveno KJ, Gilstrap LC, Hanks GD. *Williams obstetrics* 20th edition. Stamford, CT: Appleton and Lange. 1997.
6. Morrison I, Olsen J. Weight-specific stillbirths and associated causes of death: an analysis of 765 stillbirths. *American journal of obstetrics and gynecology*. 1985 Aug 15;152(8):975-80.
7. Fretts RC, Boyd ME, Usher RH, Usher HA. The changing pattern of fetal death, 1961-1988. *Obstetrics and gynecology*. 1992 Jan;79(1):35-9.
8. Pitkin RM. Fetal death: diagnosis and management. *American journal of obstetrics and gynecology*. 1987 Sep 1;157(3):583-9.
9. Özcan a, Mehmet k, Kopuz ay, Turan v, Özeren m. Intrauterin ölü doğum olgularında önlenebilir risk faktörlerinin belirlenmesi. *Bozok Tıp Dergisi*. 2015;5(1):32-6.
10. Jacobsson B, Ladfors L, Milsom I. Advanced maternal age and adverse perinatal outcome. *Obstetrics & Gynecology*. 2004;104(4):727-33.
11. Huang L, Sauve R, Birkett N, Fergusson D, van Walraven C. Maternal age and risk of stillbirth: a systematic review. *Canadian Medical Association Journal*. 2008;178(2):165-72.
12. Gordon A, Raynes-Greenow C, McGeechan K, Morris J, Jeffery H. Risk factors for antepartum stillbirth and the influence of maternal age in New South Wales Australia: A population based study. *BMC pregnancy and childbirth*. 2013;13(1):1.
13. Penn N, Oteng-Ntim E, Oakley LL, Doyle P. Ethnic variation in stillbirth risk and the role of maternal obesity: analysis of routine data from a London maternity unit. *BMC pregnancy and childbirth*. 2014;14(1):1.
14. Group SCRNW. Association between stillbirth and risk factors known at pregnancy confirmation. *JAMA: the journal of the American Medical Association*. 2011;306(22).
15. Addo V. Body mass index, weight gain during pregnancy and obstetric outcomes. *Ghana medical journal*. 2010;44(2).
16. Whiteman VE, Crisan L, McIntosh C, Alio A, Duan J, Marty PJ, et al. Interpregnancy body mass index changes and risk of stillbirth. *Gynecologic and obstetric investigation*. 2011;72(3):192-5.
17. Smith GC. Sex, birth weight, and the risk of stillbirth in Scotland, 1980–1996. *American journal of epidemiology*. 2000 Mar 15;151(6):614-9.
18. Mondal D, Galloway TS, Bailey TC, Mathews F. Elevated risk of stillbirth in males: systematic review and meta-analysis of more than 30 million births. *BMC medicine*. 2014;12(1):1.
19. Bukowski R, Hansen NI, Willinger M, Reddy UM, Parker CB, Pinar H, et al. Fetal growth and risk of stillbirth: a population-based case-control study. *PLoS Med*. 2014;11(4):e1001633.
20. Cnattingius S, Haglund B, Kramer MS. Differences in late fetal death rates in association with determinants of small for gestational age fetuses: population based cohort study. *Bmj*. 1998;316(7143):1483.
21. Nakamura MU, Alexandre SM, Santos JFKd, Souza Ed, Sass N, Beck APA, et al. Obstetric and perinatal effects of active and/or passive smoking during pregnancy. *Sao Paulo Medical Journal*. 2004;122(3):94-8.
22. Aliyu MH, Wilson RE, Alio AP, Kristensen S, Marty PJ, Whiteman VE, et al. Association between tobacco use in pregnancy and placenta-associated syndromes: a population-based study. *Archives of gynecology and obstetrics*. 2011;283(4):729-34.
23. Marufu TC, Ahankari A, Coleman T, Lewis S. Maternal smoking and the risk of still birth: systematic review and meta-analysis. *BMC public health*. 2015;15(1):1.
24. Health UDo, Services H. *The health consequences of smoking: a report of the Surgeon General*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. 2004;62.
25. Mihaila C, Schramm J, Strathmann FG, Lee DL, Gelein RM, Luebke AE, et al. Identifying a window of vulnerability during fetal development in a maternal iron restriction model. *PLoS One*. 2011;6(3):e17483.
26. Abeysena C, Jayawardana P, SENEVIRATNE DA. Maternal hemoglobin level at booking visit and its effect on adverse pregnancy outcome. *Australian and New Zealand Journal of Obstetrics and Gynaecology*. 2010;50(5):423-7.
27. Stephansson O, Dickman PW, Johansson A, Cnattingius S. Maternal hemoglobin concentration during pregnancy and risk of stillbirth. *Jama*. 2000;284(20):2611-7.
28. Seyom E, Abera M, Tesfaye M, Fentahun N. Maternal and fetal outcome of pregnancy related hypertension in Mettu Karl Referral Hospital, Ethiopia. *Journal of ovarian research*. 2015;8(1):1.
29. Nicholson J, Kellar L, Ahmad S, Abid A, Woloski J, Hewamudalige N, et al. USA Term Stillbirth Rates and the 39-Week Rule: a cause for concern? *American Journal of Obstetrics and Gynecology*. 2016.