## Research Article

# The Relationship between Non-Genetic Risk Factors and Miscarriage at Dr. Hasan Sadikin and Bandung Kiwari General Hospital

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**Abstract**
**Objective:** This study aims to analyze the relationship between non-genetic risk factors and miscarriage at Dr. Hasan Sadikin and Bandung Kiwari General Hospital in the period January – December 2025.
**Method:** This case-control study analyzed pregnant women with miscarriage. Cases were selected using total sampling, and controls using random sampling with a 1:1 ratio. Data was collected from medical records, maternal health records, and questionnaires. Analysis was performed using univariate analysis, bivariate analysis using the Chi-square or Fisher exact test, and multivariate analysis using Firth's penalized logistic regression. Data processing was performed using IBM SPSS version 31.0.
**Result:** This study results indicate that the majority of patients with miscarriage were mostly aged 20—35 years and 25.1% of them had a history of miscarriage in a previous pregnancy. There were four non-genetic factors that were independently associated with miscarriage after adjustment for potential confounding factors; maternal age over 35 years (aOR 2.74, p <0.001), anemia (aOR 16.61, p <0.001), alcohol consumption (aOR 12.72, p=0.02), and strenuous physical activity (aOR 13.48, p=0.02).
**Conclusion:** Advanced maternal age, anemia, alcohol consumption, and strenuous physical activity were associated with miscarriage. These non-genetic risk factors should be considered in the screening and monitoring of pregnant women to reduce the risk of pregnancy complications.

**Keywords**: Miscarriage, non-genetic, reproductive health, risk factors

# Hubungan antara Faktor Risiko Non-Genetik dan Abortus di RSUP Dr. Hasan Sadikin Bandung dan RSUD Bandung Kiwari

**Abstrak**
**Tujuan:** Penelitian ini bertujuan menganalisis hubungan antara faktor risiko non-genetik dan abortus di RSUP Dr. Hasan Sadikin dan RSUD Bandung Kiwari periode Januari – Desember 2025.
**Metode:** Penelitian *case-control* ini menganalisis ibu hamil dengan abortus. Sampel kasus diambil menggunakan *total sampling* dan kontrol menggunakan *random sampling* dengan rasio 1:1. Data dikumpulkan melalui rekam medis, buku KIA, dan kuesioner. Analisis dilakukan secara univariat, bivariat (uji Chi-square atau Fisher exact), dan multivariat (Firth's *penalized logistic regression*). Data diolah menggunakan perangkat lunak IBM SPSS versi 31.0.
**Hasil:** Hasil penelitian menunjukkan bahwa pasien dengan abortus sebagian besar pada rentang usia 20−35 tahun dan 25,1% diantaranya memiliki riwayat abortus pada kehamilan sebelumnya. Terdapat empat faktor non-genetik yang berhubungan secara independen dengan abortus setelah penyesuaian terhadap faktor-faktor perancu potensial, yakni usia ibu lebih dari 35 tahun (aOR 2.74, p <0.001), anemia (aOR 16.61, p<0.001), konsumsi alkohol (aOR 12.72, p = 0.02), dan aktivitas fisik berat (aOR 13.48, p =0.02).
**Kesimpulan:** Usia ibu lanjut, anemia, konsumsi alkohol, dan aktivitas fisik berat berhubungan dengan abortus. Faktor-faktor risiko non-genetik tersebut perlu menjadi perhatian dalam skrining dan pemantauan ibu hamil untuk menurunkan risiko komplikasi kehamilan.

**Kata kunci:** Abortus; faktor risiko; kesehatan reproduksi; non-genetik

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## Introduction

Miscarriage is the termination of a pregnancy occurring at a gestational age of less than 20 weeks or with a fetal weight of less than 500 grams, when the fetus is not yet viable outside the uterus, resulting in fetal death and maternal complications.[1,2] Miscarriages can be classified into spontaneous and induced miscarriages.[3] Spontaneous miscarriage occurs without a definite cause, whereas induced miscarriage is the intentional termination of a pregnancy through specific interventions.[4,5]

Miscarriage is a highly undesirable event, yet its incidence remains quite high globally, reaching 23 million cases per year.[6,7] In Indonesia, research across several hospitals indicates an upward trend in the incidence of miscarriage over the past few years, rising from 8.14% into 22.9% in 2020−2022.[1,8] Sixty percent of miscarriages occur between 6−10 weeks of gestation. The most common cause is fetal chromosomal abnormalities. Other contributing factors include advanced maternal age, obesity, a history of previous miscarriage, and a history of vaginal bleeding during the first trimester.[9,10]

Although numerous studies have analyzed risk factors associated with miscarriage, evidence regarding the distribution and magnitude of non-genetic risk factors among pregnant women in Bandung remains unclear. Most prior studies were conducted in different populations and settings; their findings may not be directly generalizable to the local population due to variations in sociodemographic characteristics and maternal health profiles. This gap in local evidence limits our understanding of whether factors identified in other populations exhibit similar relationships. This study aims to identify and quantify the relationships between non-genetic risk factors and miscarriage among women receiving obstetric care at Dr. Hasan Sadikin General Hospital and Bandung Kiwari General Hospital, Indonesia. These two hospitals were selected because they serve as major referral centers in Bandung City and handle a high volume of obstetric and gynecological cases, thereby providing access to a sufficient study population.

## Method

This study used an observational analytic case-control design. The study was conducted at Dr. Hasan Sadikin and Bandung Kiwari General Hospital from February 1st to April 30th, 2026; using data from pregnancies managed during January−December 2025. The study population comprised pregnant women with gestational age <20 weeks who received care at either study site during the study period. The case group: pregnant women who experienced miscarriage, whereas the control group: pregnant women from the same population who did not experience miscarriage. Eligible participants were women with sufficient medical record data and/or maternal health record (Buku KIA) data to assess the non-genetic risk factors investigated in this study. Women whose medical records were unavailable or lacked essential information required for assessment were excluded. The study received ethical approval under approval number DP.04.03/D.XIII.13/264/2026.

All eligible miscarriage cases identified during the study period were included using total sampling; no separate sample size calculation was performed for this group. The control group was selected at a 1:1 ratio with the case group using simple random sampling. For control selection, all eligible controls from the same population and study period were identified to form a sampling frame, assigned unique identification numbers, and selected using computer-generated random numbers until the required sample was reached.

Data on non-genetic risk factors were collected retrospectively from medical records, maternal health records, and a structured questionnaire. After eligible cases and controls was identified from the medical records, participants were contacted and invited to complete the questionnaire to obtain information that was not available in the medical records. The factors investigated included maternal age, anemia, Body Mass Index (BMI), smoking, alcohol consumption, physical activity, diabetes mellitus, and other predefined maternal factors. Each risk factor was classified according to its operational definition specified in the study protocol. Exposure assessment was based on information available before the occurrence of miscarriage. Anemia was determined based on the hemoglobin level documented at the first antenatal examination before the occurrence of miscarriage. BMI were identified based on anthropometric measurements before pregnancy, a BMI <18.5 kg/m² or ≥25.0 kg/m² was categorized as malnutrition. The "smoking" category includes patients who are active and/or passive smokers. Physical activity is categorized as strenuous if it involves lifting 11 kg during pregnancy.

Data was entered into Microsoft Excel and analyzed using IBM SPSS Statistics 31.0. Binary categorical variables were coded as 0 and 1, with 0 representing the reference category. Univariate analysis was performed using frequencies and percentages. Bivariate analysis was conducted to assess the relationship using odds ratios (ORs) and 95% confidence intervals (CIs). The Chi-square test or Fisher's exact test was used as appropriate based on the expected cells count. Variables with sparse data or zero cells were analyzed using Fisher's exact test for categorical comparisons. Candidate variables for multivariate analysis were selected based on clinical and epidemiological relevance as potential confounders, supported by findings from the bivariate p-value < 0.25. Multivariate analysis was performed using Firth's penalized logistic regression to identify factors independently associated with miscarriage, it was used to address potential complete or quasi-complete separation associated with sparse predictors. Multicollinearity among variables included in the multivariate model was assessed using variance inflation factor (VIF) and tolerance values. A VIF < 5 was considered to indicate no substantial multicollinearity.

## Result

This study involved 860 participants: 430 mothers who had experienced a miscarriage and 430 who had not. Participant characteristics are described in Table 1.

**Table 1 Participant Characteristics**

| Characteristics | Frequency (n) | Presentation (%) |
|---|---|---|
| Age | | |
| 10−19 years | 116 | 13.5% |
| 20−35 years | 634 | 73.7% |
| >35 years | 110 | 12.8% |
| Anemia | | |
| Yes | 57 | 6.6% |
| No | 803 | 93.4% |
| Body Mass Index (BMI) | | |
| Normal | 778 | 90.5% |
| Malnutrition | 82 | 9.5% |
| Nutritional status based on BMI | | |
| Underweight | 10 | 1.2% |
| Normal | 778 | 90.5% |
| Overweight | 25 | 2.9% |
| Obesity | 47 | 5.5% |
| Smoking history | | |
| Yes | 311 | 36.2% |
| No | 549 | 63.8% |

| Characteristics | Frequency (n) | Presentation (%) |
|---|---|---|
| Alcohol consumption | | |
| Yes | 7 | 0.8% |
| No | 853 | 99.2% |
| Strenuous physical activity | | |
| Yes | 5 | 0.6% |
| No | 855 | 99.4% |
| Hepatitis B | | |
| Positive | 3 | 0.3% |
| Negative | 857 | 99,7% |
| HIV | | |
| Reactive | 3 | 0.3% |
| Non-reactive | 857 | 99.7% |
| Syphilis | | |
| Reactive | 6 | 0.7% |
| Non-reactive | 854 | 99.3% |
| History of previous miscarriage(s) | | |
| Yes | 216 | 25.1% |
| No | 644 | 74.9% |
| History of X-ray examinations during pregnancy | | |
| Yes | 0 | 0% |
| No | 860 | 100% |
| History of diabetes mellitus | | |
| Yes | 11 | 1.3% |
| No | 849 | 98.7% |
| History of emesis gravidarum | | |
| Yes | 67 | 7.8% |
| No | 793 | 92.2% |
| Total | 860 | 100% |

Table 1 shows that the majority of women who experienced a miscarriage were aged 20–35 years, with a minimum age of 16 and a maximum of 46, and a mean age of 27.3 years. Among the women, 6.6% had anemia and 9.5% suffered from malnutrition. Additionally, 36.2% were smokers (active and/or passive), 0.8% consumed alcohol during pregnancy, and 0.6% engaged in strenuous physical activity. Regarding medical conditions, 0.3% had hepatitis B, 0.3% had HIV, and 0.7% had syphilis. 25.1% of participants had a history of previous miscarriage, 1.3% had a history of diabetes mellitus, and 7.8% had a history of emesis gravidarum. No participants in either group reported undergoing X-ray examination during pregnancy; therefore, this variable was not included in the bivariate or regression analyses due to the lack of variability in exposure status.

Table 2 shows that maternal age over 35 years was associated with a higher odd of miscarriage compared to the adolescent and reproductive age groups. Anemia was associated with higher odds of miscarriage compared to the absence of anemia. Abnormal nutritional status; whether underweight, overweight, or obese, was associated with higher odds of miscarriage, although this is not statistically significant ($p = 0.64$). Alcohol consumption during pregnancy was significantly associated with miscarriage ($p = 0.01$), whereas smoking was not ($p = 0.07$). However, the odds ratio (OR) of alcohol consumption, strenuous physical activity, and HIV status could not be estimated because 100% of patients with these habits experienced a miscarriage.

The history of reactive Hepatitis B and syphilis test was associated with a higher odd of miscarriage, though these findings are not statistically significant. The history of miscarriage was associated with a higher odd of miscarriage in subsequent pregnancies, a finding that is statistically significant ($p < 0.001$). The history of diabetes mellitus was associated with higher odds of miscarriage compared to having no history of the condition, and this relationship is statistically significant ($p = 0.03$).

There was no missing data among the

**Table 2 Relationship between Non-Genetic Risk Factors and Miscarriag**

| Non-genetic risk factorS | Miscarriage (n) | No miscarriage (n) | OR (95%CI) | p value |
|---|---|---|---|---|
| Age | | | | |
| 10−35 years | 350 | 399 | 2.94 (1.89−4.56) | <0.001 |
| >35 years | 80 | 31 | | |
| Anemia | | | | |
| Yes | 54 | 3 | 20.4 (6.33−65.9) | <0.001 |
| No | 376 | 427 | | |
| Body Mass Index (BMI) | | | | |
| Normal | 387 | 391 | 1.11 (0.70−1.75) | 0.64 |
| Malnutrition | 43 | 39 | | |
| Smoking history | | | | |
| Yes | 168 | 143 | 1.28 (0,97−1.70) | 0.07 |
| No | 262 | 287 | | |
| Alcohol consumption | | | | |
| Yes | 7 | 0 | Not estimable | 0.01 |
| No | 423 | 430 | | |
| Strenuous physical activity | | | | |
| Yes | 5 | 0 | Not estimable | 0.06 |
| No | 425 | 430 | | |
| Hepatitis B | | | | |
| Positive | 2 | 1 | 2.00 (0.18−22.1) | 0.56 |
| Negative | 428 | 429 | | |
| HIV | | | | |
| Reactive | 3 | 0 | Not estimable | 0.25 |
| Non-reactive | 427 | 430 | | |
| Syphilis | | | | |
| Reactive | 5 | 1 | 5.05 (0.59−43.3) | 0.10 |
| Non-reactive | 425 | 429 | | |
| History of previous miscarriage(s) | | | | |
| Yes | 129 | 87 | 1.69 (1.23−2.31) | <0.001 |
| No | 301 | 343 | | |
| History of diabetes mellitus | | | | |
| Yes | 9 | 2 | 4.57 (0.98−21.3) | 0.03 |
| No | 421 | 428 | | |
| History of emesis gravidarum | | | | |
| Yes | 29 | 38 | 0.74 (0.45−1.23) | 0.25 |
| No | 401 | 392 | | |
| Total | 860 (100%) | 860 (100%) | | |

**Table 3 Multivariate Analysis of Non-Genetic Risk Factors Associated with Miscarriage**

| Variables | Adjusted OR (aOR) | 95%CI | p value |
|---|---|---|---|
| Age >35 years | 2.74 | 1.75−4,39 | <0.001 |
| Anemia | 16.61 | 6.37−60.95 | <0.001 |
| Smoker | 1.23 | 0.92−1.66 | 0.16 |
| Alcohol consumption | 12.72 | 1.41−1677.4 | 0.02 |
| Strenuous physical activity | 13.48 | 1.48−1781.1 | 0.02 |
| Reactive syphilis | 3.24 | 0.54−33.62 | 0.20 |
| History of previous miscarriage | 1.33 | 0.95−1.87 | 0.10 |
| History of diabetes mellitus | 2.86 | 0.73−15.75 | 0.14 |

variables included in the multivariate analysis; therefore, no imputation was performed. The Firth's penalized logistic regression model converged successfully after 1000 iterations. Table 3 presents the results of the multivariate analysis; the age group over 35 years, anemia, alcohol consumption, and strenuous physical activity were associated with higher odds of miscarriage and were statistically significant. However, the estimates for alcohol consumption and strenuous physical activity lack precision, as indicated by the wide confidence intervals. These results are consistent with the sparse data and the zero cells observed previously. No substantial multicollinearity was identified among the variables included in the multivariate analysis, with VIF values ranging from 1.005 to 1.081 and tolerance values ranging from 0.925 to 0.995.

## Discussion

This study shows that, in the univariate analysis, the majority of pregnant women who experienced a miscarriage were within the reproductive age range, and approximately one-quarter had a history of miscarriage in a previous pregnancy. Bivariate analysis revealed that age, anemia, alcohol consumption, history of previous miscarriage, and history of diabetes mellitus were associated with miscarriage. These findings represent crude associations without adjustment for other covariates. In multivariate analysis, after adjustment for potential confounding factors, advanced maternal age, anemia, alcohol consumption, and strenous physical activity remained independently associated with miscarriage.

In this study, maternal age over 35 years was significantly associated with miscarriage, with an adjusted odds ratio (aOR) of 2.74 ($p < 0.001$). This finding is consistent with a previous study by Ozawa N et al., which reported a mean maternal age of 37.9 years among 364 participants and found a significant relationship between advanced maternal age and abnormal karyotypes ($p<0.001$).[11] Advanced maternal age has been associated with changes in fertility and reproductive lifespan among women over the age of 35, characterized by a reduction in oocyte quality. In addition to a decrease in quantity, oocyte quality also declines, affecting meiotic division and chromosome segregation, which ultimately leads to implantation failure and spontaneous miscarriage.[12,13]

In this study, anemia was significantly associated with miscarriage, with an increased odds of miscarriage observed among women with anemia. This finding is consistent with previous studies conducted by Larasati FD et al. and Sabrina R et al., which reported that anemia may be related to an increased likelihood of miscarriage by four- to six-fold.[14,15] A previous study by Zakira S. et

al. also reported a significant relationship between low hemoglobin concentration and the occurrence of miscarriage ($p = 0.02$). Among the 12 respondents in their study, four pregnant women with anemia did not experience a miscarriage, whereas the other eight did (5% versus 20%, respectively). This study, involving a larger number of participants, showed that three of the 57 anemic patients did not experience a miscarriage, whereas the other 54 did (5.3% versus 94.7%). Several mechanisms have been proposed to explain this relationship. Anemia causes a deficiency in the oxygen and nutrients that hemoglobin is supposed to deliver to all body tissues. This reduced supply affects not only the mother but also the fetus, thereby disrupting fetal development in the womb and increasing the risk of miscarriage.[16–18]

In this study, alcohol consumption during pregnancy was found to be significantly associated with miscarriage ($p < 0.001$). This finding aligns with research by Sundermann AC et al., which indicated that alcohol exposure during pregnancy carries higher odds of miscarriage compared to no exposure (OR 1.19). The risk of miscarriage increases with the number of alcoholic drinks consumed.[19] Other research by Sundermann AC et al. also indicates that alcohol consumption between 5−10 weeks of gestation increases the odds of spontaneous miscarriage. The risk of spontaneous miscarriage rises by 8% (aHR 1.08) with advancing gestational age and alcohol consumption. Alcohol exposure leads to miscarriage through alterations in maternal hormone levels, changes to biochemical pathways during embryogenesis, inhibition of retinoic acid synthesis, and disruption of epigenetic programming.[20]

In this study, strenuous physical activity was significantly associated with miscarriage, with an aOR of 13.48 ($p = 0.02$). Physical activity is categorized as “strenuous” if a pregnant woman lifts a single load weighing ≥11 kg; this cut-off value follows previous studies by Certenais T et al. and Cai C et al. These studies have demonstrated an association between heavy lifting during pregnancy and miscarriage (OR 1.31).[21,22] This finding is also consistent with a previous study by Sejbaek et al., which found that 13% of 1.9 million pregnant women exposed to a high physical workload during pregnancy experienced a miscarriage.[23] Research studies by Cai C. et al. and Francis F. et al. also indicate that miscarriage is associated not only with physical activities involving heavy lifting but also with standing for prolonged periods and long working hours.[22,24]

A limitation of this study is that it did not analyze risk factors such as socioeconomic status and the quality of antenatal care (ANC) due to data constraints within the registry records. The case-control study design and recruitment from two hospital-based settings may have introduced selection bias, as the characteristics of pregnant women receiving care at these hospitals may differ from those of pregnant women in the general population. The retrospective use of medical records may also have resulted in incomplete or inconsistent documentation of some exposures. Additionally, because some exposure information was obtained through questionnaires administered after the pregnancy outcome, recall bias cannot be excluded, particularly for self-reported behavioral and lifestyle factors. Exposure misclassification is also possible if participants inaccurately recalled the timing or frequency of exposures. Although exposure assessment was intended to reflect the period before miscarriage, the retrospective nature of data collection may have introduced temporal ambiguity for some variables when the exact timing of exposure relative to the outcome could not be established with certainty.

Additionally, some variables had small sample sizes, resulting in sparse-data bias and potentially unstable ORs. Although

multiple miscarriage non-genetic risk factors were analyzed simultaneously, residual confounding from unmeasured factors, including socioeconomic characteristics and the quality of ANC, cannot be excluded. As an observational study, it cannot directly establish causal relationships between variables. Furthermore, because the study was conducted at only two hospitals in Bandung, which serve specific referral populations, the findings may not be fully generalizable to pregnant women in other healthcare settings or regions. Nevertheless, the study utilizes real data and provides local evidence regarding non-genetic risk factors associated with miscarriage among women receiving care at the two study hospitals. The findings can be used to improve screening for pregnant women of advanced maternal age and those with anemia.

## Conclusion

This study demonstrates that after adjustment for potential confounding factors, advanced maternal age, anemia, alcohol consumption, and strenuous physical activity were independently associated with miscarriage. The risk factors associated with miscarriage in this study warrant special attention during the screening and monitoring of pregnant women.

## Suggestions

The findings of this study are expected to serve as a reference for healthcare professionals when identifying and screening pregnant women with risk factors for miscarriage, thereby enabling more intensive pregnancy monitoring and the earliest possible intervention regarding modifiable risk factors. Future researchers are encouraged to employ prospective or cohort designs and to include larger sample sizes as well as a broader range of risk variables.

## Ethical Approval

This study received ethical approval from the Health Research Ethics Committees at Dr. Hasan Sadikin and Bandung Kiwari General Hospital. Patients or their families, who met the study criteria received a verbal explanation and consented to participate in the study by signing an informed consent form.

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## Artificial Intelligence (AI) Usage Statement

The researchers did not use AI tools in the preparation, drafting, analysis, development, or writing of this manuscript.

## Author Contribution Statement

MA contributed to the conceptualization of the study, data collection, data analysis, and manuscript drafting. DA and RKP contributed to study supervision, interpretation of results, and manuscript revision. All authors reviewed and approved the final manuscript and agreed to be responsible for all aspects of this research.

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## Conflict of Interest

The authors state that they have no conflicts of interest regarding this study.

**Data Availability Statement**

The data supporting the findings of this study are not publicly available due to privacy and confidentiality considerations regarding patient information. The data may be obtained from the corresponding author upon reasonable request and subject to applicable ethical and institutional restrictions.

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