



Risk Factors of Ectopic Pregnancy at Dr. Kariadi Hospital

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ABSTRACT

Background: Ectopic pregnancy leads to maternal death. There were several risk factors for ectopic pregnancy, including age, IUD, parity, history of ectopic pregnancy, history of pelvic and abdominal surgery, infertility, history of PID, history of abortion, and infertility treatment.

Objective: This study aims to prove the correlation between these factors and ectopic pregnancy at RSUP Dr. Kariadi.

Methods: This study was an analytical observational study with case-control design that consisted of 134 samples, divided into ectopic pregnancy (n=67) and imminent abortion as controls (n=67), collected from patient medical records from 2019 – 2024 using *purposive sampling*. Data analysis was carried out using bivariate analysis with Chi Square & Fisher Exact Test and multivariate analysis with Logistic Regression Test.

Results: There was a correlation between history of ectopic pregnancy ($p = 0.034$), history of abortion ($p = 0.002$), and infertility ($p = 0.009$) with ectopic pregnancy. Other variables did not have significant relationship with ectopic pregnancy ($p > 0.05$). Two risk factors were identified for ectopic pregnancy: history of abortion ($p = 0.001$; aOR = 3.52; 95% CI 1.85 – 6.70) and infertility ($p = 0.005$; aOR = 2.91; 95% CI 1.56 – 5.43).

Conclusion: There was a significant correlation between history of ectopic pregnancy, history of abortion, and infertility with ectopic pregnancy, while other variables were not related to ectopic pregnancy. Both history of abortion and infertility were risk factors for ectopic pregnancy.

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1. Introduction

Maternal mortality rate (MMR) is the number of deaths of women caused by pregnancy-related complications, during childbirth, or within the postpartum period (up to 42 days after delivery), per 100,000 live births. It is one of the standards of public health in a country. MMR in Indonesia has declined from previous years to 189 in the 2020 population census, which means 189 maternal deaths per 100,000 live births. Compared to the 2010 population census, the maternal MMR has decreased by 45%.¹ This figure is almost close to the 2024 National Medium-Term Development Plan (RPJMN) MMR target of 183, but still far from the Sustainable Development Goals (SDGs) target. WHO targets a global MMR of less than 70 per 100,000 live births by 2030 per SDG target 3.1.²

Central Java has an MMR of 84.60/100,000 live births, which is better than the RPJMN target for 2024. This must be reduced to meet the SDGs target. Most maternal deaths in Central Java are caused by hypertension, bleeding, circulatory disorders, infections, COVID-19, metabolic system disorders, and other causes. Hemorrhage was the second most common, with a percentage of 19.91%.³ One of the causes of bleeding in the first trimester of pregnant women is an ruptured ectopic pregnancy.

Ectopic pregnancy occurs in 7.93% of all gynecological cases.⁴ Ectopic pregnancy is an event where the conception result is not embedded normally in the mother's uterine wall but in another location, which does not have a structure that can support the pregnancy process. The larger the size of the conception that grows and develops outside the uterus, the more likely it can cause organ rupture and bleeding, called an ruptured ectopic pregnancy. This can reduce the vital condition of the mother, cause organ damage, and even death. Ectopic pregnancy is the leading cause of maternal death in the first trimester, accounting for 10-15% of all maternal mortality.⁵

Ectopic pregnancy has various risk factors, including maternal age over 35 years, intrauterine device (IUD) use, previous ectopic pregnancy, history of pelvic and abdominal surgery, history of infertility, pelvic inflammatory disease, smoking, history of tubal surgery, assisted reproduction technology, and history of abortion.⁶⁻⁹

Research on risk factors for the incidence of ectopic pregnancy has been done, but has not been done at Dr. Kariadi Hospital.^{8,10,11} In connection with this, the researcher is interested in conducting a study to analyze the risk factors for ectopic pregnancy at Dr. Kariadi Hospital, Semarang.

2. Methods

This study is an analytic observational research with a case-control research design. The study was conducted in the medical record installation of Dr. Kariadi Hospital Semarang in May-June 2024. The study subjects were patients with ectopic pregnancy as cases and non-ectopic pregnancy as controls, and had met the inclusion and exclusion criteria, with a total of 67 each. Control subjects were selected from patients with intrauterine pregnancies who were diagnosed with imminent abortion, as they had similar gestational age with the case group. Inclusion criteria were treatment at Dr. Kariadi Hospital Semarang in 2019-2024. Exclusion criteria were incomplete medical records. The independent variables in this study were age, parity, IUD, history of ectopic pregnancy, history of pelvic and abdominal surgery, history of infertility, history of pelvic inflammatory disease, history of abortion, and history of infertility treatment. The dependent variable was ectopic pregnancy. Data collection was done by purposive sampling. The collected data will be processed and analyzed by a computer program. Data analysis was performed using bivariate analysis and multivariate analysis. Bivariate analysis uses Chi-Square test or Fisher Exact test to analyze the relationship between variables. Then, multivariate analysis was performed with logistic regression test.

3. Result

Based on 134 medical records, there were 67 cases and 67 controls. Table 1 shows the characteristics of age, sociodemographics (latest education, occupation, regional origin), parity, infertility, gestational age, complaints, Hb levels, blood transfusion requirements, length of hospitalization, and admission to ICU. There were no patients who presented with shock.

Table 1. Characteristics of the Research Sample

Variables	Ectopic Pregnancy (n=67)		Non-Ectopic Pregnancy (n=67)	
	n	%	n	%
Age				
<20	0	0	1	1.49
20-35	58	86.57	58	86.57
>35	9	13.43	8	11.94
Education				
Elementary School	4	5.97	3	4.48
Junior High School	7	10.45	4	5.97
Senior High School	37	55.22	35	52.24
Diploma/Graduate	19	28.36	25	37.31
Occupation				
Public employee	35	52.24	35	52.24
Private employee	5	7.46	15	22.39
Self-employed	8	11.94	1	1.49
Not working	19	28.36	16	23.88
Origin				
Semarang	34	50.75	49	73.13
Out of Semarang	33	49.25	18	26.87
BMI				
Underweight	4	5.97	5	7.46
Normal	28	41.79	21	31.34
Overweight	12	17.91	17	25.37
Obesity grade 1	14	20.89	19	28.36
Obesity grade 2	9	13.43	5	7.427
Parity				
Nulliparous	33	49.25	33	49.25
Primiparous	24	35.82	20	29.85
Multiparous	10	14.93	14	20.89
Infertility				
Primary infertility	8	11.94	5	7.46
Secondary infertility	29	43.28	16	23.88
No	30	44.77	46	68.66
Gestational age				
< 8 weeks	33	49.25	26	38.81
>8 weeks	34	50.75	41	61.19
Abdominal pain				
Yes	53	79.10	41	61.19
No	14	20.86	26	38.81
Vaginal bleeding				
Yes	50	74.63	58	86.57
No	17	25.37	9	13.43
Low Back Pain				
Yes	4	5.97	0	0
No	63	94.03	67	100
Shock				
Yes	0	0	0	0
No	67	100	67	100
Hb levels				
Severe anemia	0	0	0	0
Moderate anemia	8	11.94	3	4.48
Mild anemia	12	17.91	5	7.46
No anemia	47	70.15	59	88.06
Blood Transfusion				
Yes	14	20.90	3	4.48
No	53	79.10	64	95.52
Length of Stay				
<3 days	51	76.12	57	85.07
> 3 days	16	23.88	10	14.93
Admitted to ICU				
Yes	2	2.99	0	0
No	65	97.01	67	100

Table 2 shows the characteristics of ectopic pregnancy based on location, right/left direction, occurrence of rupture, surgical procedures and methods performed, and bleeding that occurred. The majority of patients had ectopic pregnancies in the tubal ampulla at 83.58%. There were ovarian, abdominal, and heterotropic pregnancies at 1.49%,

2.99%, and 1.49%. The procedure that was often performed was laparotomy at 83.58%.

Table 2. Characteristics of Ectopic Pregnancy

Variables	Frequency (n=67)	Distribution (%)
Ectopic Pregnancy Location		
Tubal ampulla	56	83.58
Tubal isthmus	6	8.96
Tubal fimbriae	1	1.49
Ovary	1	1.49
Abdomen	2	2.99
Heterotopic	1	1.49
Ectopic Pregnancy Directors (adnexa)		
Right	39	60
Left	26	40
Rupture		
Rupture	33	49.25
Not yet ruptured	34	50.75
Procedure		
Laparotomy	56	83.58
Laparoscopy	11	16.42
Methods		
Salpingectomy	38	56.72
Salpingostomy	21	31.34
Salpingo-oophorectomy	1	1.49
Uterine cornu resection	3	4.48
Fimbriectomy	1	1.49
Partial oophorectomy	1	1.49
Exploration for fetus extraction	1	1.49
Resection of abdominal pregnancy mass	1	1.49
Bleeding		
≤100 cc	40	59.70
>100 cc	27	40.30

The results of the bivariate analysis between several variables and ectopic pregnancy are shown in Table 3. There was a significant association between abortion, primary & secondary infertility, and ectopic history with ectopic pregnancy.

Table 3. Bivariate Analysis

Variables	Ectopic Pregnancy (n=67)		Non-Ectopic Pregnancy (n=67)		cOR	p
	n	%	n	%		
Age						
< 20 & > 35 years	9	13.4	9	13.4	1	1 [§]
20 – 35 years	58	86.6	58	86.6		
Parity						
Nulliparous & Primiparous	57	85.1	53	79.1	1.51	0.499 [§]
Multiparous	10	14.9	14	20.9		
Abortion						
Yes	34	50.7	16	23.9	3.28	0.002 ^{§*}
No	33	49.3	51	76.1		
IUD						
Yes	0	0	5	7.5	–	0.058 [§]
No	67	100	62	92.5		
Infertility						
Yes	37	55.2	21	31.3	2.70	0.009 ^{§*}
No	30	44.8	46	68.7		
History of ectopic pregnancy						
Yes	10	14.9	2	3	5.70	0.034 ^{§*}
No	57	85.1	65	97		
History of Pelvic Inflammatory Disease (PID)						
Yes	0	0	0	0	–	–
No	67	100	67	100		
History of pelvic and abdominal surgery						
Yes	23	34.3	23	34.3	1.00	1.000 [§]
No	44	65.7	44	65.7		
ART						
Yes	0	0	2	3	2.03	0.496 [§]
No	67	100	65	97		

Notes : * Significant (p < 0.05); [§] Continuity Correction; [§] Fisher's exact

The results of the multivariate analysis between several variables are shown in Table 4. There were 2 significant risk factors for ectopic pregnancy, abortion and infertility. Abortion has the greatest risk of 3.516, while infertility has a risk of 2.913 for ectopic pregnancy. The results of the aOR of abortion and infertility which are greater than the cOR, indicate that there is an additive relationship from other variables, which means that there is a mutually reinforcing interaction with other variables.

Table 4. Multivariate Analysis

Variables	P	aOR	90% CI
Abortion	0.001*	3.52	1.85 – 6.70
Infertility	0.005*	2.91	1.56 – 5.43
History of ectopic pregnancy	0.198	2.96	0.74 – 11.87

Notes : * Significant (p < 0.05)

4. Discussion

The degree of nasal obstruction in the control group in this study showed an increase in nasal obstruction that was not statistically significant (p > 0.05), as indicated by the increase in the average NOSE Scale value and the decrease in the average PNIF value. This occurred because the control group did not receive nasal irrigation.

The relationship between maternal age and ectopic pregnancy at Dr. Kariadi Hospital Semarang in this study showed insignificant results based on the bivariate test results. These results are in line with previous studies by Pradana but contradict studies by Triana et al.^{10,12} Other studies also contradict this study which states that older age indicates that there is an increased risk of ectopic pregnancy, age more than 39 years has a risk of 9.05 times while age 33-38 years has a smaller risk of 4.3 times.⁸ Most of the ectopic pregnancy samples were in the age range of 20 to 35 years, as much as 86.57%. This is in line with two previous studies, which showed that the age ranges of 24 to 34 years and 20 to 35 years have the greatest tendency to the occurrence of ectopic pregnancy.^{13,14} The high frequency of samples with an age range of 20 to 35 years, which is the peak of reproductive age and has a high probability of conception, increases the incidence of ectopic pregnancy if there is tubal infertility.¹³ Women in this age group have higher sexual activity, are more prone to sexually transmitted diseases and end up with pelvic inflammatory disease or tubal infection, which can be one of the risks of ectopic pregnancy.^{10,15}

The use of IUD contraceptives does not have a significant relationship with ectopic pregnancy at Dr. Kariadi Hospital Semarang. Previous research conducted by Ramadhan et al & Li et al showed the opposite results.^{7,16} Previous research states that current IUD use that fails to prevent pregnancy is at risk of ectopic pregnancy by 16.43 times.⁷ The use of IUDs reduces the risk of ectopic pregnancy compared to women who do not use them because IUDs are effective in preventing pregnancy.¹⁷ In

case of pregnancy with IUD use, ectopic pregnancy is more likely than intrauterine pregnancy by 53%.^{17,18} The use of IUDs of both levonorgestrel and copper types that experience ectopic pregnancy is much less (0.5% and 0.46%) than women without contraceptive use (6.9%).¹⁸

There was no significant association between parity and ectopic pregnancy at Dr. Kariadi Hospital Semarang. This study is not in line with previous research by Arifuddin et al.¹⁹ Nulliparous women had a higher percentage (49.25%) than primiparous and multiparous women in this study, which is thought to occur due to cases of primary infertility that may occur due to abnormal fallopian tubes.²⁰ Whereas in primiparous and multiparous women who have given birth, it shows that there is no disturbance in the tubes, both in terms of function and mechanics, so the ovum can implant in the uterine cavity.²⁰

There is a significant association between history of ectopic pregnancy and the incidence of ectopic pregnancy, but did not significantly risk ectopic pregnancy after multivariate analysis. Previous studies on the history of ectopic pregnancy showed influential results with a risk of 6.34.⁹ The recurrence of ectopic pregnancies indicates that there are functional disorders, damage to the tubes, or the formation of scar tissue during healing will cause adhesions in the lumen that can interfere with the passage of conception results to the uterine cavity.^{9,20,21} This may be due to the ectopic pregnancy itself or its management, such as salpingostomy.²⁰

There was no significant association between history of pelvic and abdominal surgery with ectopic pregnancy. This contradicts previous studies, which suggest that pelvic and abdominal surgeries, including tubal surgery and appendectomy, are at risk of ectopic pregnancy.^{6,9,22} Previous pelvic and abdominal surgeries are associated with scar formation from connective tissue that causes adhesions in the tubes and peritoneal cavity.^{22,23} Previous caesarean section is associated with infection, disruption of the placental attachment site, and formation of adhesions that are at risk of ectopic pregnancy. Previous studies stated that the incidence of recurrent ectopic pregnancy was lower in the group that underwent salpingectomy compared to salpingostomy.^{20,24}

There was a significant relationship between infertility status and the incidence of ectopic pregnancy. The relationship between infertility status alone has a risk of 2.70 times for ectopic pregnancy. Multivariate analysis showed that infertility is a risk factor for ectopic pregnancy and has a joint risk with other variables for the incidence of ectopic pregnancy of 2.91 times. This result is similar to previous research which states that infertility has a 3.14 times risk of ectopic pregnancy.⁹ Previous studies have stated that primary infertility has a greater risk of secondary infertility.⁸ Infertility has a risk of ectopic pregnancy due to tubal damage or mechanical obstructions in the fallopian

tubes that hinder the motility of conception to the uterus.^{20,25} A history of PID, previous ectopic pregnancy, and history of surgery can lead to infertility.²⁰ Women with infertility who undergo infertility treatment may also increase the risk of ectopic pregnancy.²⁰ The result of aOR greater than cOR indicates that other variables strengthen the influence of infertility on the incidence of ectopic pregnancy.

The variable pelvic inflammatory disease was not recorded in the medical records therefore, the variable could not be analyzed. Pelvic inflammatory disease is an infection of the reproductive organs that can increase the risk of ectopic pregnancy by 13.2 times based on previous research.²⁶ PID can cause inflammation of the fallopian tubes, then scarring occurs in the fallopian tubes, which can interfere with the passage of conception to the uterus.²⁷ The function of cilia and smooth muscles that help push the egg to the uterus is also disrupted.^{28,29}

Abortion was significantly associated with ectopic pregnancy. Multivariate analysis showed that abortion was the most influential variable on ectopic pregnancy, with a risk of 3.52 times. Previous research showed similar results, abortion had a risk of 1.91 times the incidence of ectopic pregnancy.⁹ Another study stated that the more often abortion occurs, the higher the risk of abortion for recurrent ectopic pregnancy.²⁰ Abortion, both spontaneous and induced, as well as complications from its management, can cause damage to the endometrium, which can lead to scars. Improperly managed abortion can increase the risk of PID.²⁰ Hormonal changes and immunological factors can increase the risk of ectopic pregnancy but need to be studied further. The odds ratio result of the bivariate test was 3.28, while the multivariate test was 3.52, which indicates that there is an association of other variables that strengthen the risk of abortion to ectopic pregnancy.

Infertility treatment was not found in the cases but present in 3% of the controls, that in line with previous research, which states that the presence of imminent abortion has a higher incidence than ectopic pregnancy after In Vitro Fertilization-Embryo Transfer (IVF-ET).³⁰ In this study, the relationship between infertility treatment and ectopic pregnancy showed no significant results. Previous studies have shown different results, infertility treatments, especially Assisted Reproductive Therapy (ART), have 8.83 times higher incidence of ectopic pregnancy.³¹ Multiple embryo transfers tend to increase the risk of ectopic pregnancy compared to transferring only one embryo because other embryos can attach in the wrong place.³² Another mechanism is that the embryo is transferred accidentally into the fallopian tube, resulting in tubal ectopic pregnancy.²⁹ The infertility treatment procedure itself can damage the tubes, which increases the risk of ectopic pregnancy.^{20,29}

This study is a retrospective study in which the data collected is only based on medical records, which could be an information bias and selection bias. This study categorized infertility status based on medical records, including length of time married, length of time not pregnant, and contraceptive use, not considering the assumption that the sample wanted to delay pregnancy either, with or without natural family planning methods, which need to be asked directly.

5. Conclusion

There was a significant association between history of previous ectopic pregnancy, abortion, and infertility with ectopic pregnancy. Other variables were not found to be associated with ectopic pregnancy. Based on the analysis, abortion and infertility were identified as risk factors, with abortion emerging as the dominant risk factor in this study.

Ethical Approval

Ethical clearance was obtained from Komisi Etik Penelitian Kesehatan (KEPK) of the Faculty of Medicine, Diponegoro University Semarang with No. 172/KEPK/FK-UNDIP/IV/2024.

Conflicts of Interest

The authors declare no conflict of interest.

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Author Contributions

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