# **OVERVIEW OF BLIGHTED OVUM CASES**

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#### ABSTRAK

Blighted ovum atau kehamilan anembrionik merupakan keadaan dimana seorang wanita hamil namun tidak terdapat janin didalam kandungannya, dikarenakan ovum yang dibuahi tidak berkembang. Hingga saat ini penyebab kejadian blighted ovum belum dapat dideteksi karena gejala yang tidak spesifik. Umumnya kejadian blighted ovum terjadi pada trimester I dan memungkinkan untuk terulang kembali pada kehamilan selanjutnya. Tujuan penelitian ini untuk mengetahui gambaran kejadian blighted ovum. Metode penelitian yang digunakan adalah Literature Review yang didapatkan dari 3 database yaitu PubMed, ResearchGate dan Google Scholar dengan kriteria inklusi jurnal terakreditasi Sinta dan Scopus. Hasil penelitian dari 5 jurnal didapatkan karakteristik berdasarkan usia, paritas, imunologis, dan kelainan genetik pada ibu hamil yang mengalami blighted ovum. Kesimpulan: Ibu hamil yang mengalami blighted ovum memiliki karakteristik usia >40 tahun dengan paritas multigravida dan grandemultigravida, memiliki kelainan imunologi dan genetic.

#### ABSTRACT

Blighted ovum or anembryonic pregnancy is a condition where a woman is pregnant but there is no fetus in her womb, because the fertilized ovum does not develop. Until now, the cause of blighted ovum cannot be detected because the symptoms are not specific. Generally, blighted ovum occurs in the first trimester and allows it to recur in subsequent pregnancies. The purpose of this study was to describe the incidence of blighted ovum. The research method used was Literature Review which was obtained from 3 databases namely PubMed, ResearchGate and Google Scholar with the inclusion criteria of Sinta and Scopus accredited journals. The research results from 5 journals obtained characteristics based on age, parity, immunological, and genetic abnormalities in pregnant women who experienced blighted ovum. Conclusion: Pregnant women who experience blighted ovum have characteristics of age> 40 years with multigravida and grandemultigravida parity, have immunological and genetic disorders.

#### **INTRODUCTION**

Pregnancy is a natural (physiological) process (Yuliani et al, 2021). Some pregnancies occur with certain conditions that are not common, one of which is blighted ovum. Blighted ovum is also known as an anembryonic pregnancy, which is where the gestational sac develops normally but the fertilized egg does not develop into an embryo (Mitwally et al., 2018). Blighted ovum often occurs early in pregnancy, even very early, because the symptoms are difficult to know with certainty (Sulistyowati et al. (2017). One of the consequences that can arise from a blighted ovum is an event that is likely to recur in subsequent pregnancies (Nuzul ZA & Rosdiana, 2019).

According to WHO (2012) Around 60% of premature miscarriages worldwide are caused by blighted ovum. Based on ASEAN data, the incidence of blighted ovum reaches 51% and is found in 37% of every 100 pregnancies in Indonesia (Nurlelawati et al., 2019). The incidence of blighted ovum is the second leading cause of early miscarriage, which is 37.5% in a previous research study involving 17,810 early trimester pregnant women who experienced blighted ovum (Sinensis et al.

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2020). In one of the studies conducted by Nurlelawati (2019) also stated the same thing that the prevalence of blighted ovum was around 52% in pregnant women in the first trimester (0-12 weeks).

Some people sometimes associate the blighted ovum with mystical things. Some who said their pregnancy was lost were carried by spirits or their babies were transferred to other people, etc. This indeed gives the impression that the baby has suddenly disappeared, without knowing that the mother actually has a blighted ovum (Sutomo, 2010 in Rahmawati, 2021). Blighted ovum can be diagnosed through ultrasound examination by assessing the development of the embryo. Women who experience blighted ovum generally also feel signs of pregnancy including delayed menstruation, nausea, vomiting, cravings, enlarged abdomen, enlarged breasts and even a positive pregnancy test (Yeni et al, 2018).

Providing pre-conception education and counseling in planning subsequent pregnancies is important in efforts to prevent subsequent pregnancy failures (Yeni et al, 2018) by knowing the description of blighted ovum events which are one of the complications of pregnancy, so the authors are interested in conducting research through literature review entitled "Descriptive Study of Blighted Ovum Events".

### **METHODS**

The research design used is the traditional Literature Review. The literature search used data based on an international scale, such as Pubmed and Research Gate as well as a national scale from Google Scholar which met the researcher's inclusion criteria.

## **RESULT AND DISCUSSION**

Table 1 frequency distribution of blightedovum events based on age

	Years		Age						
Journal article	of Publica tion	Sample	< 20		20 - 35		> 40		
			( <b>f</b> )	%	(f)	%	(f)	%	
Prevalence of blighted									
ovum in first trimester of	2019	280	10	17,1	39	50	78	77,5	
pregnancy Blighted Ovum in Sub fertile Patients Undergoing Assisted Reproductive Technology	2017	147					33.57		

(Mitwally et al., 2019) (Qing Wen et al. 2017)

Table 1 shows the results of a literature review of five articles, two of which show the age characteristics of pregnant women who experience blighted ovum, which are more common at ages > 40 years.

The results of the literature review show that the age characteristic of pregnant women who experience blighted ovum is > 40 years. In the study by Mitwally et al. (2019) showed the same thing, that is, more pregnant women who experience blighted ovum are >40 years old. In the research by Qing Wen et al. (2017) also showed that elderly mothers can increase the risk of blighted ovum.

Age is the length of a person's life which is calculated based on the time of birth, the biological development of the human body's organs develops according to the course of age (Wink-josastro, 2016 in Rahmawati, 2021). When the mother starts to enter the age of 30, the mother's fertility will decrease, where the decrease in fertility affects the quality of the eggs produced each time ovulation (Sukarni, 2014 in Rahmawati, 2021). According to the WHO, the peak of the fertile period and the best quality of egg cells for women is at the age of 20-30 years. This is because at the age of <20 years the female reproductive organs are not fully mature, whereas the increasing age of a woman can affect the quality of egg cells or sperm cells which allows blighted ovum to occur.

Table 2: frequency	distribution of blighted
ovum events	based on parity

					-	-				
	Years		Parity							
Terroral continue	of		1		2	- 5	> 5			
Journal article	Public	sampie	(f)	%	(f)	%	(f)	%		
	ation									
Prevalence of										
blighted ovum in	2019	280	74	26.5	127	45.5	79	28		
first trimester of				,-						
pregnancy										

(Nurlelawati et al., 2019)

Table 2 above is the result of a literature review of five articles, one of which shows that pregnant women who experience blighted ovum based on parity characteristics are more common in women with multigravida parity and second place in pregnant women with grandemultigravida parity.

The results of the literature review show that the characteristics of pregnant women who experience blighted ovum are that most have multigravida parity and grand multigravida parity. In a study by Mitwally et al., (2019) showed that pregnant women who experienced blighted ovum were more likely to occur in women with multigravida parity and some occurred in grandemultigravida mothers. In another study, Nurlelawati et al, (2019) showed the same thing that pregnant women who experienced blighted ovum were more likely to have parity 2-4 and parity > 5.

Based on the theory of Apriyani et al, (2022) Parity is the number of births that produce live or dead fetuses. Multiparas are women who have given birth to live children no more than five times, while grandemultiparas are women who have given birth to fetuses more than 5 times. So that the more the number of births experienced by a mother, the higher the risk of experiencing pregnancy complications (Rahmawati, 2021).

Table 3 frequency distribution of blightedovum events based on parity

Journal	Years of publicati on	Samp le	Immunological disorders Mean (%)			
			HLA-E	NK Cells		
Blighted ovum: Roles of human leukocyte antigen-E and natural killer cells	2017	32	75.15	93.88		

(Sulistyowati et al., 2017)

In table 3, the results of a literature review of five articles found that one article showed that pregnant women who experienced blighted ovum had characteristics of immunological disorders with a lower average HLA-E and a higher average of NK cells.

The results of the literature review on the study of Sulistyowati et al. (2017) showed that there are immunological abnormalities in pregnant women who experience blighted ovum. Human Leukocyte Antigen (HLA) is thought to play an important role in maintaining the products of conception. The mean Human Leukocyte Antigen-E (HLA-E) expression in the blighted ovum group was lower than in the normal pregnancy group, while the expression of Natural Killer (NK) cells was higher in the blighted ovum group.

According to theory (Yeni et al, 2018) Miscarriage is the result of immunological activation in response to the presence of Immunological pathological organisms. factors play a role in the occurrence of abortion, where almost all blighted ovum can be detected after a miscarriage. Immunological factors play a role through cellular and humoral response mechanisms against certain of organs pregnant women, such as incompatibility of the HLA (Human Leukocyte Antigen) system. HLA-E has an important role as a mother's immune tolerance in the development of pregnancy. HLA-E is expressed on trophoblast cells which can help

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the fetus avoid maternal immune intolerance (Sulistyowati et al, 2017). If HLA-E is not expressed, the ability of trophoblast cells will be reduced and prevented from invading the uterus because they are considered non-self which has antigen properties that trigger the formation of antibodies in the mother resulting in failure of conception products. HLA-E can help the fetus from attacks by the mother's immune system, HLA-E which is not expressed can make the fetus more vulnerable to attack by the expression of NK cell activity which is higher than HLA-E and results in blighted ovum.

# Table 4 frequency distribution of blightedovum events based on Genetic disorder

Journal	Years of publicati on	Sam ple	Genetic Diorder					
			CC		CT		TT	
			(f)	%	(f)	%	(f)	%
Polymorphism of MnSOD (Vall 6Ala) gene in pregnancies with blighted	2017	34	1	2	17	50	16	48
ovum Relationship between HLA- DPA1 genetic polymorphism and an embryonic pregnancy	2019	190	21	43,8	15	25	20	57,1

(Moshtaghi et al., 2017) (Zhendong et al., 2019)

In table 4, the results of a literature review of five articles, 2 of which showed that pregnant women who experienced blighted ovum had genetic abnormalities, namely the MnSOD polymorphism, the heterozygous genotype (CT) was more than the homozygous genotype. Whereas in the HLA-DPA1 polymorphism the number of homozygous genotypes (CC + TT) is higher than the heterozygous genotypes. This shows that polymorphism in both variants has a high value for each variant. This high presentation can disrupt the balance of polymorphism and result in damaged DNA cells. So that genetic variation can increase the risk of anembryonic pregnancy.

The results of a literature review in the study of Zhendong et al., (2019) showed a genetic abnormality in the HLA-DPA1 polymorphism, where the homozygous variant (rs1431403) of this polymorphic locus (CC and TT) is

involved in increasing abnormal HLA-DPA1 expression which can increase the increase the risk of developing an anembryonic pregnancy. Human leukocyte antigen (HLA)-DP is an HLA class II molecule. Overexpression of class II HLA molecules in placental trophoblastic cells can cause miscarriage. In the study of Mostaghi et al., (2017) also showed the same thing but in a different polymorphic, namely the Val/Ala (CT) genotype in the polymorphic MnSOD gene. Manganese superoxide dismutase (MnSOD) is an important antioxidant enzyme in the human immune system. The gene is located on chromosome 6q25 and acts on the mitochondrial matrix. In case of mutation or inactivity of this enzyme, mitochondrial and nuclear DNA will be severely damaged. The most common polymorphism of the gene is Val/Ala (CT). The most important function of MnSOD is its role in scavenging peroxide free radicals to produce H2O2 and O2. The resulting H2O2 will then be decomposed into water by GPX1 and catalase. So if the percentage of MnSOD is high, it can disrupt the balance of the three enzymes, so if there is an imbalance between the three enzymes and the concentration of H2O2, this can harm the DNA cells inside. According to the theory (Yeni et al, 2019) that genetic chromosomal abnormalities of the parents and several immunological factors are associated with anembryonic pregnancies. Chromosomal abnormalities that most often cause recurrent miscarriages are balanced translocations which cause trisomy conceptions. Single gene disorder can be identified by careful examination of family history or by identifying patterns of abnormalities known as hereditary patterns. This is in line with the results of a study (Sinesis et al, 2020) that genetic factors are the most common factor causing blighted ovum.

## CONCLUSION

Based on the identification results from five journals through a literature review process, it was found that the characteristics of pregnant women who experienced blighted ovum, namely pregnant women aged > 40 years, multi parity and grand multigravida, had immunological disorders as well as genetic abnormalities.

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