# **Systematic Review**

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# The relationship between Apgar score and gender with the incidence of neonatal sepsis: systematic review

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#### **ABSTRACT**

Neonatal sepsis is a cause of mordibity and mortality in newborns that causes long-term complications that can lead to death. One of risk factors for neonatal sepsis in infants is the Apgar score and gender. The aim of the study was to analyze the relationship between Apgar score and gender with the incidence of neonatal sepsis. This study was systematic review, in searching sourced from six databases (EBSCO, Clinicalkey Nursing, PubMed, ProQuest, Science Direct and Springer Link). In searching for studies using the PICOS framework, the selection study used The Joanna Brigss Guideline Critical Appraisal. The literature used was 14 studies. The results of this study were from 14 literatures used, the average total incidence of neonatal sepsis was 0.356 (35.6%).10 of the 14 literatures stated that the 5th minute Apgar score of less than seven (<7) could be an independent predictor of the risk of neonatal sepsis with a mean risk of 16.9% (p value<0.01) and there were 8 from 14 literatures which states that there is a significant relationship between gender and the incidence of male gender morbidity with a risk of 1.02 (p value=0.00). The results showed that there was a relationship between Apgar scores and gender with the incidence of neonatal sepsis. Therefore, nurses or birth attendants need to be vigilant and take preventive measures if they find babies have Apgar scores and male sex as signs of a possible higher risk of neonatal sepsis in newborns.

Keywords: Apgar score, Gender, Sepsis, Neonatal

## INTRODUCTION

Infection is a health problem that often occurs in developed and developing countries. Infection knows no age, race and gender, anyone can experience this health problem even in newborns. Infection in newborns less than 28 days of life is known as neonatal sepsis. Neonatal sepsis is a disease caused by systemic bacterial infection, this infection is a major cause of morbidity and mortality in newborns. <sup>2</sup>

The results of The Global Burden of Disease (2016) study identified neonatal sepsis as a cause of newborn death. the third most common and the 16th largest contributor to death in all age groups and there are 336,300 deaths per year caused by neonatal sepsis.<sup>3</sup> In Indonesia, the

incidence of neonatal sepsis is 8.7%-30.29% with a mortality rate of 11.56%-40.9%.

Neonatal sepsis can cause complications of infant growth and development delays, communication delays and developmental delays pervasive developmental disorder not otherwise specified (PDD-NOS), developmental delays caused by sepsis can continue until the child is 5 years old if not treated.<sup>5</sup>

Sepsis is influenced by various factors, namely maternal, environmental and infant factors. One of the risk factors for infants is the Apgar score and gender, but there is a difference of opinion on the Apgar score and gender as factors that influence the incidence of neonatal sepsis, therefore the purpose of this study was to analyze the

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relationship between the Apgar score and the type of pregnancy with the incidence of neonatal sepsis.

#### **METHODS**

The research method used in this study is a systematic review. Secondary data obtained and used in this study were in the form of international journal articles and books with a predetermined theme, namely the relationship between Apgar score and gender with the incidence of neonatal sepsis. The literature search in this study used 6 databases that had high and medium quality criteria, including the EBSCO database, Clinicalkey Nursing, PubMed, ProQuest, Science Direct and Springer Link, or, not) is used to expand or specify in the search, making it easier to determine the journal that will be used as a framework in preparing the review. The keywords in this study are in accordance with Medical Subject Heading (MeSH), namely Apgar score and gender and sepsis neonatorum. The next journal article selection process by reading the entire article and re-selecting articles that do not fit will be discarded and will be recorded using the PRISMA flow chart strategy. Selected journal articles will be extracted independently by three researchers and examined by other researchers. The results of the selection of articles are described in the Flow Diagram (Figure 1).

The results of a literature search found 18 journals which were then assessed using The Joanna Brigss Guideline (JBI) Critical Appraisal by following a checklist according to the research design in the literature, critical appraisal was used to help limit the possibility of post hoc bias in a systematic review so as to get reviews that are in accordance with research purposes. The literature used is literature that has a quality result value of >50% with characteristics that are included in accordance with a predetermined protocol. Researchers conducted an assessment using JBI critical appraisal, there were 14 literatures that did not have the risk of bias and could used, the results of the study assessment using The JBI critical appraisal tools (Table 1).

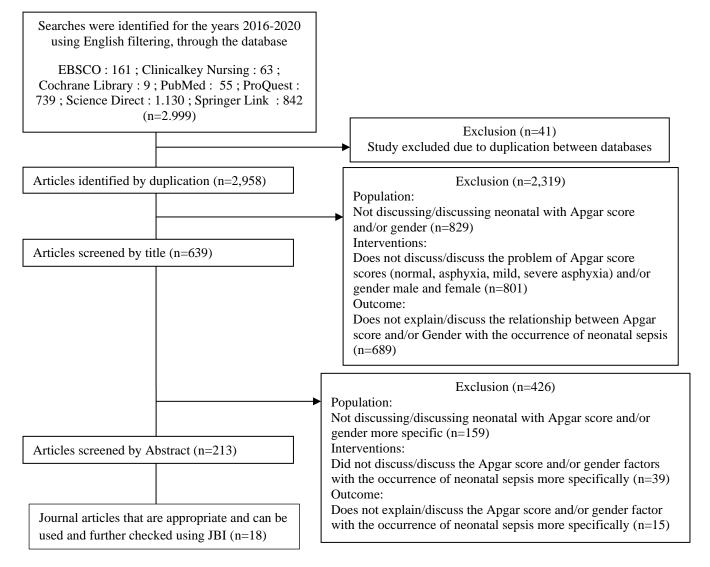


Figure 1: Relationship between Apgar score and gender with the incidence of neonatal sepsis.

Table 1: Result of study assessment for systematic review using the JBI critical appraisal tools.

Ctude ID	As	sessi	nent	crite	ria							Result
Study ID	1	2	3	4	5	6	7	8	9	10	11	Result
Cohort study												
Ndombo et al, 2017		$\sqrt{}$			$\sqrt{}$					$\sqrt{}$	$\sqrt{}$	10/11 (90,9%)
Gutbir et al, 2020		$\sqrt{}$						$\sqrt{}$		$\sqrt{}$	$\sqrt{}$	10/11 (90,9%)
Schindler et al, 2017											$\sqrt{}$	11/11 (100%)
Garfinkle et al, 2020										$\sqrt{}$	$\sqrt{}$	11/11 (100%)
Voskamp et al, 2020											$\sqrt{}$	10/11 (90,9%)
Case control study												
Akalu et al, 2020												9/10 (90,9%)
Boghossian et al, 2018										$\sqrt{}$		10/10 (100%)
Gebremedhin et al, 2016		$\sqrt{}$			$\sqrt{}$					$\sqrt{}$		10/10 (100%)
Stevic et al, 2018												9/10 (90,9%)
Al-Matary et al, 2019					$\sqrt{}$					$\sqrt{}$		9/10 (90,9%)
Systematic review and meta	Systematic review and meta-analysis											
Bitew et al, 2020		$\sqrt{}$			$\sqrt{}$					$\sqrt{}$	$\sqrt{}$	11/11 (100%)
Murthy et al, 2019		$\sqrt{}$						$\sqrt{}$		$\sqrt{}$	$\sqrt{}$	11/11 (100%)
Cross sectional study												
Hospital et al, 2020												8/8 (100%)
Ibishi et al, 2018	V							V				7/8 (90,9%)

#### **RESULTS**

Based on Table 2 of study characteristics in 14 journal articles, it was found that from the total the average incidence of neonatal sepsis was 0.356 (35.6%) and the average number of non-septic events was 0.643 (64.3%). In 14 journal articles listed from the literature assessed as obtained from Voskamp et al (2020) the highest yield of samples diagnosed with sepsis returned 895,272 (51.4%) from 1,742,831 neonates and in the hospital literature had the lowest sample yield. diagnosed with sepsis found 21 (25.9%) of 81 neonates.<sup>8</sup> The results of the analysis based on the p value Apgar score and gender to determine the relationship between the Apgar score and gender with the incidence of neonatal sepsis are included in Table 3.

In the research results of Gutbir et al it is stated that an Apgar score with a low score is at risk of experiencing neonatal sepsis with a relative risk of 1.28, in line with the results of research from 9 literatures discussing Apgar scores with a low score can be 3 times greater risk to suffer from neonatal sepsis (p value<0.05, 95% CI: 1.3-7-7, OR: 3.2).<sup>1,9-16</sup> Assessment of the Apgar score can be done at the same time as the examination of sex, gender is one of the risk factors for neonatal sepsis. The gender at risk for infection is higher in the male sex, this is in accordance with the results of the study of Murthy, et al that male infants are 1.3 times higher risk of infection (p value=0.03, 95% CI: 1.02-1.68, OR: 1.3) compared to female infants, this is in line with the results of 5 literature studies which state that male sex is at risk 1.31 (p value=0.003, 95% CI: 1.22-1.41, OR: 1.31) had a higher risk of infection and even death than women. 13-15,17-19

Table 3 shows the results of the analysis that 10 of the 14 literatures that discuss the Apgar score, the results of research from 10 literatures that the 5th minute Apgar score value of less than seven is an independent predictor of the risk of neonatal sepsis with a p value<0.01 (95% CI: 8.31-41.45, OR: 18.56) with a mean risk of 16.9%. 1,9,13 A low Apgar score at minute 5 has a risk of 3.47 times more likely to be infected (p value=0.000, 95% CI: 2.53-4.41, OR: 3.47) and even cause death, compared to newborns born with Apgar normal scores. 15 The 1st minute Apgar score with a value less than 7 has a 1.5 times greater risk of infection (p value=0.01, 95% CI: 5.7-0.99). 16

There is a difference in risk values between the Apgar score for values less than 7 seen at the 1st minute and seen from the 5th minute, this is because asphyxia causes immunological disorders and requires resuscitation intervention after birth, this tends to give time for bacteria to have the opportunity to explore self in newborns. 12 Table 3 shows that there is a significant relationship between gender and the occurrence of morbidity in the male sex with a relative risk of 1.20 (p value=0.001, 95% CI: 1.02-1.40, RR: 1.40), this study is in line with 7 other studies which state that there is a significant relationship between the occurrence of infection and gender but the results of the study by Ndombo et al showed that gender was not associated with the occurrence of neonatal sepsis (p value=0.4621). 10,12,18 The male sex that tends to be at risk for becoming a risk factor for neonatal sepsis is the sex born <30 weeks because in infants born <30 weeks, the biological development of the fetus is still immature compared to the female sex.<sup>19</sup>

**Table 2: Characteristics of the included studies.** 

						Sample					
S.	Study	Location	Study period	Setting	Study design	Sepsis		No-sepsis		Sample size (N)	Risk factor
no.						N	%	N	%	(14)	
1.	Ndombo et al, 2017	Cameroon	11 November 2015 to 29 February 2016	Neonatology unit	Cohort study	104	31.3	228	68.6	332 neonates	Apgar score
2.	Gutbir et al, 2020	Israel	January 1991 to January 2014	Database Soroka University Medical Center (SUMC)	Cohort study	238	1	223.006	99	223.244 neonates	Apgar score
3.	Schindler et al, 2017	New South Wales dan Australia Capital Territory	1 January 2007 to 31 December 2011	NICUS	Cohort study	1.505	33.7	2.949	66.3	4.454 neonates	Apgar score and baby with male gender
4.	Garfinkle et al, 2020	Canada	January 2007 to December 2016	NICUS	Cohort study	3.667	21.8	13.144	78.2	16.811 neonates	Baby with male gender
5.	Voskamp et al, 2020	Saudi Arabia	January 2011 to December 2015	NICU	Cohort study	895.272	51.4	847.559	48.6	1.742.831 neonates	Baby with male gender
6.	Akalu et al, 2020	Northwest Ethiopia	March 2018 to April 2018	NICU	Case control study	77	33.3	154	66.7	231 neonates	Apgar score
7.	Boghossian et al, 2018	United States	1 January 2006 to 31 December 2016	NICU	Case control study	38.465	18.7	167.285	81.3	205.750 neonates	baby with male gender
8.	Gebremedhin et al, 2016	North \Ethiopia	December 2014 to June 2015	IMNCI (Intergrated Management of neonatal and childhood illness)	Case control study	78	33.3	156	66.7	234 neonates	Apgar score
9.	Stevic et al, 2018	Belgrade	December 2005 to December 2015	NICU	Case control study	35	47.3	39	52.7	74 neonates	Apgar score and baby with male gender
10.	Al-Matary et al, 2019	Saudi Arabia	January 2011 to December 2015	NICU	Case control study	245	45.1	298	54.9	245 neonates	Apgar score and baby with male gender
11.	Bitew et al, 2020	Sub- Saharan Africa	June 2020	Web of Science, PubMed, Elseiver, Scopus, CINAH, World Cat dan Google scholar	Systematic review and metaanalysis	14.756	3.3	431.143	96.6	445.899 neonates	Apgar score and baby with male gender

Continued.

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S.	Study	Location	Study period	Setting	Study design	Sample Sepsis		No-sepsis		Sample size (N)	Risk factor
110.						N	%	N	%	(14)	
12.	Murthy et al, 2019	India	March 2000 to March 2018	PubMed, CINAH, Scopus, Web of Science, Popline, Indmed, Indian Science Abstract dan Google scholar	Systematic review and meta-analysis	4.850	9.2	48.274	90.8	53.124 neonates	Baby with male gender
13.	Hospital et al, 2020	Pakistan	October 2015 to December 2016	NICU	Cross sectional studies	21	25.9	60	70.1	81 neonates	Apgar score and baby with male gender
14.	Ibishi et al, 2018	Kosovo	September 2013 to July 2015	Obstetri Clinic dan Ginekologi Tersier	Cross sectional studies	26	14	174	86	200 neonates	Apgar score
Resu	lts					959.339		1.734.469		2.693.808	
Aver	age					0.356		0.643			

Table 3: Relationship between Apgar score and gender with the incidence of neonatal sepsis.

C	C4J	Hypothesis test results					
S. no.	Study	P value	95% CI	OR/RR			
		Apgar score					
1.	Ndombo et al, 2017	<0.01	8.31-41.45	RR:18.56			
1.	Nuomoo et al, 2017	Male gender					
		0.4621	0.69-2.28	RR:1.25			
		Apgar score					
2.	Gutbir et al, 2020	0.04	1.01	RR:1.28			
2.	Guion et al, 2020	Male gender					
		0.003	1.08-1.48	RR.1.27			
		Apgar score					
3.	Schindler et al, 2017	0.000	1.34-2.13	RR:1.69			
3.	Schildler et al, 2017	Male gender					
		0.000	4.56-7.18	RR.5.73			
		Male gender					
4.	Garfinkle et al, 2020	0.01	0.96-1.09	RR.1.02			
7.	Garrinkie et al, 2020	Apgar score					
		-	-	-			
5.	Voskamp et al, 2020	Male gender					
J.	v Oskanip et al, 2020	0.0001	1.02-1.40	RR.1.20			

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		Apgar score		
		-	-	-
		Apgar score		
6.	Akalu et al, 2020	< 0.05	1.3-7.7	OR:3.2
U.	Akaiu et al, 2020	Male gender		
		-	<del>-</del>	<del>-</del>
		Male gender		
7.	Boghossian et al, 2018	< 0.001	1.06-1.10	OR: 1.08
/•	Dognossian et al, 2018	Apgar score		
		-	-	-
		Apgar score		
8.	Gebremedhin et al, 2016	< 0.001	3.63-13.08	OR;68.9
0.	Gebremediini et al, 2016	Male gender		
		< 0.001	0.44-0.91	OR: 0.44
		Apgar score		
0	S4	0.04	5.71-2.09	OR: 5.46
9.	Stevic et al, 2018	Male gender		
		0.03	27-8	OR:5.32
		Apgar score		
10.	A1 Marana et al. 2010	0.02	48.5-58.5	OR:48.5
10.	Al-Matary et al, 2019	Male gender		
		0.01	45.5-57.7	OR: 45.5
		Apgar score		
11.	Bitew et al, 2020	0.000	2.53-4.41	OR: 3.47
11.		Male gender		
		0.003	1.22-1.41	OR:1.31
		Male gender		
12.	Months of al 2010	0.03	1.02-1.68	OR:1.3
12.	Murthy et al, 2019	Apgar score		
		-	<del>-</del>	-
		Apgar score		
12	Hamital at al. 2020	<0.001	-	-
13.	Hospital et al, 2020	Male gender		
		<0.001	-	-
1.4	Think at al. 2019	Apgar score		
14.	Ibishi et al, 2018	0.01	5.7-0.99	-

#### **DISCUSSION**

Neonatal sepsis is an infectious process experienced by infants aged less than 28 days of life with signs of systemic infection syndrome, circulatory shock and multisystem organ failure.<sup>2</sup> The incidence of neonatal sepsis continues to increase every year, seen from the incidence of neonatal sepsis from 2016-2020 when added up to 939,768 cases of sepsis in the last 5 years.<sup>18,9,15,18,20</sup>

The incidence of neonatal sepsis is more vulnerable in premature infants because it is seen from the immature body immunity so that this also affects the occurrence of infection.

The risk factors for neonatal sepsis are divided into three parts, one of which is the baby factor, namely the Apgar score and gender. Six studies said that a 5<sup>th</sup> minute Apgar score of less than 7 had a significant relationship with the risk of neonatal sepsis, neonates with an Apgar score of less than 7 were 3 times more likely to suffer from neonatal sepsis than those with an Apgar score of 1-5 minutes more than 7 with a p value of 0.000 (95% CI: 2.53-4.4, OR: 3.47) this is in line with Karen's theory that an Apgar score of less than 7 at minute 1 to minute 5 has a risk of infection 17.9%.<sup>21</sup>

A low Apgar score of less than 7 may reflect that the neonate has immunological disorders such as respiratory, cardiovascular and neurological disorders, therefore a low Apgar score is a signal that the neonate is at high risk of developing neonatal sepsis (95% CI: 1.01 OR: 1.28).<sup>8,9,11</sup> The results of this study are in line with Razaaz's theory that the Apgar score assessment is very important to determine whether the neonate suffers from asphyxia or not which is assessed for heart rate, respiratory effort, muscle tone, skin color (Skin Color) and reactions to stimuli (Response to Stimuli).<sup>22</sup> Gender is also one of the risk factors for neonatal sepsis. The sex most at risk for neonatal sepsis is male because men have 46XX chromosomes, this causes the X and X chromosomes to epimutate and causes the formation of Angiotensin Converting Enzme 2 (ACE2) which more than women cause vasodilating effects because they are located on cell surface receptors such as in the lungs, arteries, heart, kidneys and intestines.23

ACE2 is a viral reservoir, this causes open access for viruses and bacteria in the baby's body, resulting in the baby being more susceptible to infection or experiencing neonatal sepsis. <sup>23</sup> This is in line with five studies that say that the male sex is more susceptible to infection with a risk of 1.31 times (p value=0.003, 95% CI 2.53-4.41 OR: 1.31) This shows that gender has a value that needs to be considered in providing health action, A low Apgar score of <7 at the 1st and 5th minutes can be a signal for health workers, especially doctors, midwives and nurses that newborns can be expected to be at higher risk of developing neonatal sepsis, as well as gender, the baby's gender. The male sex who is more at risk of infection can

be a consideration for health workers to be more-wary of the occurrence of neonatal sepsis in infants. Assessment of the Apgar score and gender can also be carried out simultaneously so that it can make it easier for health workers to assess these risk factors when dealing with newborns.

### **CONCLUSION**

Apgar score and gender are risk factors for infants that can cause neonatal sepsis. Although the Apgar score assessment is still often doubted as a risk factor for neonatal sepsis because the Apgar score assessment is subjective and prone to misjudgment, the low Apgar score and male gender both contribute to the risk of neonatal sepsis. Therefore, these two risk factors need to be considered in newborns as a benchmark or signal that newborns may be at higher risk of developing neonatal sepsis, these two risk factors, Apgar score and gender can be assessed at the same time this can facilitate health workers to be able to assess quickly and accurately.

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