Systematic Review

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 morbidity 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 Briggs 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.

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. 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.

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
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 Briggs 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 according to 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).

![Diagram of the study selection process.](image-url)

**Figure 1: Relationship between Apgar score and gender with the incidence of neonatal sepsis.**
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 score, the results of the study by Ndombo et al showed that gender was not associated with the occurrence of neonatal sepsis with a p value<0.05, 95% CI: 1.3-7, OR: 3.2). 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%. 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. 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). 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=0.01, 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). 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.19
### Table 2: Characteristics of the included studies.

| S. no. | Study | Location | Study period | Setting | Study design | Sample | N | % | No-sepsis | N | % | Risk factor |
|--------|-------|----------|--------------|---------|--------------|--------|---|---|-----------|---|---|-------------|
| 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 (Intergated 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, Elsevier, Scopus, CINAHL, 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.
| S. no. | Study | Location | Study period | Setting | Study design | Sample size (N) | Risk factor |
|-------|-------|----------|--------------|---------|-------------|----------------|-------------|
| 12.   | Murthy et al, 2019 | India | March 2000 to March 2018 | PubMed, CINAHL, Scopus, Web of Science, Popline, Indmed, Indian Science Abstract dan Google scholar | Systematic review and meta-analysis | 4.850 | 53.124 neonates | Baby with male gender |
| 13.   | Hospital et al, 2020 | Pakistan | October 2015 to December 2016 | NICU | Cross sectional studies | 21 | 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 | 200 neonates | Apgar score |

### Results

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

Table 3: Relationship between Apgar score and gender with the incidence of neonatal sepsis.
|   | Study                                      | Outcome | p-Value | CI        | OR     |
|---|-------------------------------------------|---------|---------|-----------|--------|
| 6. | Akalu et al, 2020                         | Apgar score | <0.05  | 1.3-7.7   | OR:3.2 |
|   | Male gender                               |         |         |           |        |
| 7. | Boghossian et al, 2018                    | Male gender | <0.001 | 1.06-1.10 | OR: 1.08 |
|   | Apgar score                               |         |         |           |        |
| 8. | Gebremedhin et al, 2016                   | Apgar score | <0.001 | 3.63-13.08 | OR:68.9|
|   | Male gender                               |         |         |           |        |
| 9. | Stevic et al, 2018                        | Apgar score | 0.04   | 5.71-2.09 | OR: 5.46|
|   | Male gender                               |         |         |           |        |
| 10. | Al-Matary et al, 2019                     | Apgar score | 0.02   | 48.5-58.5 | OR:48.5|
|   | Male gender                               |         |         |           |        |
| 11. | Bitew et al, 2020                         | Apgar score | 0.000  | 2.53-4.41 | OR: 3.47|
|   | Male gender                               |         |         |           |        |
| 12. | Murthy et al, 2019                        | Male gender | 0.03   | 1.02-1.68 | OR:1.3 |
|   | Apgar score                               |         |         |           |        |
| 13. | Hospital et al, 2020                      | Apgar score | <0.001 | -        | -      |
|   | Male gender                               |         |         |           |        |
| 14. | Ibishi et al, 2018                        | Apgar score | 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. 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.1,8,15,18,20

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 5th 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%.21

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).8,9,11 The results of this study are in line with Razaaaz’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).22 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 Enzyme 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.23 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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