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The role of c-reactive protein as an inflammatory marker in normal postpartum: A case study at RSUD, dr. Soekardjo Tasikmalaya

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ABSTRACT

The normal delivery process is often followed by pain caused by a ruptured pervaginal wound, which can be the primary focus for assessing the degree of inflammation in the body. The presence of inflammation remains a major concern. One of the most commonly used indicators of inflammation is C-reactive protein (CRP) in response to inflammation, infections, or tissue injury. aimed at measuring CRP levels in normal postpartum patients who have been allowed to return to the hospital, Dr. Soekardjo Tasikmalaya. The samples were taken through purposive sampling and consisted of 30 patients from RSUD Dr. Soekardjo City, Tasikmalaya. The inclusion criteria in this study included patients who did not have a history of diseases such as diabetes, tuberculosis (TB), or lupus. While the exclusion criteria included the refusal of subjects to be respondents and samples who underwent hemolysis and have met the ethical test of the research with the number 043-01/E.01/KEPK-BTH/V/2024. The results of the C-reactive protein examination showed that 26 samples (86,7%) showed positive results and 4 samples (13,3%) showed negative results. So it can be concluded that normal postpartum mothers still have inflammation, especially on the first day.

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INTRODUCTION

Childbirth is a process in which the cervix opens and thins as the fetus descends into the birth pathway. Normal birth is a process of fetal production that occurs at 37-42 weeks of pregnancy, in which the fetus is born spontaneously with the head facing backwards, without any complications for mother or fetus. Cracks in the birth tract can cause bleeding in various amounts. It is important to pay attention to the source and quantity of bleeding from the birth pathway in order to be

properly treated. Sources of bleeding can come from the perineum, vagina, cervix, or rupture in the uterus. (ruptur uteri) (Pemiliana et al., 2019).

The normal delivery process is often followed by pain caused by a ruptured pervaginal wound, which can be the primary focus for assessing the degree of inflammation in the body. A perineal wound is a leakage on the urogenital diaphragm and the musculus levator ani, which occurs during normal delivery, or childbirth by instrument and can occur without injury to the skin of the perineum or to the vagina, so that it is not visible from the outside (Nurrahmaton & Sartika, 2018). Although postpartum mothers with normal conditions are usually allowed to leave the hospital shortly after delivery, the presence of inflammation is still a major concern. Signs of inflammation, i.e., redness, heat, swelling, pain, and loss of function (*functio laesa*). Pain occurs as a result of an increase in the pain mediator, both from direct damage and from the inflammatory response itself. Loss of function can occur as a result of mobility limitations caused by edema or pain or as a consequence of the replacement of cells with scar tissue (Hannood & Nasuruddin, 2024). Perineal tears occur due to tearing of the perineum during childbirth. Perineal tears are classified into four degrees. Degree I includes tears in the vaginal mucosa, posterior fourchette, and perineal skin, which generally do not require stitching if there is no bleeding and the wound is well approximated. Degree II involves tears in the vaginal mucosa, posterior fourchette, perineal skin, and perineal muscles, which require stitching. Degree III includes tears in the vaginal mucosa, posterior fourchette, perineal skin, perineal muscles, and external anal sphincter; if the birth attendant lacks the skills to repair these tears, immediate referral to a more comprehensive facility is necessary. Degree IV involves tears in the vaginal mucosa, posterior fourchette, perineal skin, perineal muscles, external anal sphincter, and anterior rectal wall. If the birth attendant lacks the skills to repair Degree IV tears, referral to a more appropriate facility must be made (Nurhayati, 2020). Wound healing is a complex physiological process involving multiple cell types, cytokines, mediators, and the vascular system. It begins with vasoconstriction and platelet aggregation to stop bleeding, followed by the arrival of inflammatory cells such as neutrophils that release mediators to promote angiogenesis, thrombosis, and reepithelialization. Fibroblasts then form extracellular components as a scaffold. Wound healing involves three main phases: inflammatory, proliferative, and maturation. The inflammatory phase involves hemostasis, chemotaxis, and increased vascular permeability and lasts several days. The proliferative phase, which can last several weeks, is characterized by the formation of granulation tissue, reepithelialization, and neovascularization. The final phase, maturation and remodeling, is when the wound reaches maximum strength and the healing process is complete. (Wallace & Zito, 2023). In this study, participants were mothers who had normal birth conditions, such as physical health of mothers who did not have serious medical conditions or significant complications during pregnancy or childbirth, such as preeclampsia, postpartum infection, or heavy bleeding, and did not have infections such as tuberculosis, systemic Lupus erythematosus, diabetes mellitus, and fever; Mental health of mothers who There are no signs of postpartum depression or other mental disorders that can affect the overall health of the mother; factors such as age during childbirth is still quite old; and the labor process that takes place without major interventions such as cesarean section.

The innate immune system plays an important role in regulating inflammatory processes. (Schmitt et al., 2021). One of the most commonly used indicators of inflammation is C-reactive protein (CRP), which is an acute phase protein produced by the liver in response to inflammation, infections, or tissue injury (Peter, 2018). CRP is the preferred serological marker for acute inflammatory conditions because of its faster kinetics and shorter half-life, leading to a rapid decrease after inflammation is overcome, making it useful not only for diagnosis but also for evaluating responses to treatment (Plebani, 2023; Cicco et al., 2020; and Buzas, 2023).

However, it is important to know how the level of CRP changes in normal postpartum mothers who have been allowed home, especially in the context of pervaginal ruptured wounds. Existing research tends to focus more on mothers with post-partum complications or who require

additional hospital care, whereas normal mothers who are returning home quickly are often not included in the study. CRP levels in postpartum women with complications are used to monitor cases of inflammation such as periodontitis (Mohr et al., 2019), gestational diabetes (Quansah et al., 2023), severity of postpartum depression symptoms, preeclampsia, premature birth, perinatal depression, autoimmune disorders (Bränn et al., 2019), and premature prenatal rupture of membranes (Mohr et al., 2019).

Therefore, this research will fill this knowledge gap by providing a more comprehensive picture of how CRP levels change in normal postpartum mothers who return home in a healthy state after the delivery process. Thus, it will better understand the inflammatory response of the body to the normal delivery process and identify the potential risk of infection or other complications that may occur in the early stages after returning home.

RESEARCH METHOD

This study is a descriptive study aimed at measuring CRP levels in normal post-partum patients who have been allowed to return to the hospital of Dr. Soekardjo Tasikmalaya. The time of blood sampling is done when the mother is allowed to go home after giving birth (on average, patients can go home 1-2 days after giving birth). If the patient is going home, blood is taken. The blood that has been taken is separated into serum and immediately examined without any delay. The samples were taken through purposive sampling and consisted of 30 patients from RSUD Dr. Soekardjo City, Tasikmalaya. The inclusion criteria in this study included patients who had no history of diseases such as diabetes, tuberculosis (Tb), and lupus, while the exclusion criteria included the refusal of subjects to be respondents and samples undergoing hemolysis. The materials used in the study include serum, latex CRP reagent, positive control serum, and negative control serums. The instruments used included a sputum, a tourniquet, an alcohol swab, a vacuum tube, gloves, centrifuges, black test slides, micropipets, yellow tips, and mixer sticks. Blood samples are taken from a peripheral vein in a common way, as done by a phlebotomy. The phlebotomy strings a rubber bracelet in the upper arm of the patient and asks the patient to hold his hand several times. After finding the appropriate vein, the phlebotomy cleans the area using an alcohol pad. After the alcohol dries, the needle is inserted into the vein to take blood into a small bottle. The rubber bracelets are removed from the patient's arm, and the needle is removed by putting pressure on the injection site to stop the bleeding, usually within about a minute (Patel, 2023). The statistical method that will be used to analyze CRP levels using SPSS statistics 21 is descriptive frequency because the results of the CRP examination used are only qualitative in the form of reactive and non-reactive, with a positive control concentration equivalent to more than 15 mg/dl. We present the data in table form, displaying percentage and frequency values.

RESULTS AND DISCUSSIONS

The study was conducted on normal postpartum mothers who were examined in the run-up to their return. A total of 30 participants were allowed to go home within one or two days of birth. The results of the CRP test can be seen in Table 1.

Table 1. CRP examination results

Result	Frequency	Percent (%)
Reactive	26	86,7
Nonreactive	4	13,3
Total	30	100,0

Based on Table 1, the CRP reactive results of 26 people consisting of postpartum mothers in the course of 1 day and 2 days. The results of the 30 samples of serum from normal postpartum patients at RSUD Soekardjo Tasikmalaya showed that of the total, 26 samples (86,7%)

showed reactive CRP test results, while 4 samples (13,3%) showed non-reactive results. Patients returned on the first day with sample codes A1, A2, A4, A6, A11, A12, A13, A14, A15, A16, A17, A18, A19, A20, A21, A22, A23, A24, A25, A26, A27, A28, A29, and A30 all showed positive results. Positive CRP results indicate that there is a concentration of CRP in the serum that indicates inflammation, infection, or tissue damage (Sproston & Ashworth, 2018). Inflammation can be caused by a rupture in the birth pathway during normal delivery, where the vagina and perineum (the area between the vaginal and anus) are prone to rupture or episiotomy. These wounds trigger local inflammation that increases the production of CRP (Mertens et al., 2019). During the preparation for childbirth, immune system cells begin migrating to the myometrium, and high levels of pro-inflammatory cytokines have been detected both in cervical tissue and peripheral blood. M1 macrophages in the uterus contribute to the inflammatory profile that promotes uterine contractions, delivery of the baby, expulsion of the placenta, and uterine involution (Bränn et al., 2019). One additional factor that can affect the positive outcome of CRP levels is postpartum infections, such as fever. Patients with the code mentioned have filled in a questionnaire that records the condition of their bodies having fever after childbirth.

In normal post-natal patients who came home on the second day with sample codes A5, A7, A9, A10, the test results were negative. Negative CRP results indicate that no concentration of CRP was detected in the serum, indicating no signs of inflammation, infection, or tissue damage. (Hannoodee & Nasuruddin, 2024). The findings are consistent with previous studies by K. Mertenz that showed CRP results in normal postpartum patients on the second day were also negative. Another factor that can accelerate wound healing is by eating proper nutrition. Good nutrition can boost the immune system and accelerate post-partum recovery. Patients who get adequate intake of nutrients are likely to have stronger immune systems, so they can fight infection or inflammation more effectively, potentially lowering their CRP levels (Fernando et al., 2021). CRP is a fairly stable protein found in serum, with a half-life of around 18 hours. Its levels rise swiftly within 4 to 6 hours after an infection, surgery, or other forms of trauma. The increase can be dramatic, ranging from a hundredfold to a thousandfold, and it reaches its peak within 48 hours (Miller & Stevens, 2021). A significant increase in serum CRP levels occurs six to eight hours after the onset of inflammation. This triggers the synthesis of CRP, which is then released into the circulation, with peak levels typically found between 24 and 48 hours due to its half-life of approximately 19 hours. So, within 2 days, CRP levels can decrease or even disappear due to its half-life of 19 hours. (Banait et al., 2022).

On sample codes A3 and A8 of the serum of the newborn patient on the second day after returning home, the result was positive. It's because the wound is still healing, so the CRP concentration is still detected. High CRP can occur during pregnancy due to the presence of preeclampsia and intrauterine growth obstruction, as well as being associated with intrauterine infection (Barawi, 2014). Meanwhile, on sample codes A5, A7, A9, and A10, the results were negative because the wound healing or tissue repair process took place faster than the A3 and A8 samples that showed positive results on CRP.

The CRP detection process is performed qualitatively using the agglutination method. The principle of the method is that the presence of C-reactive protein in the serum will be detected if it acts with human CRP antibodies attached to the latex particles present in the reagent. These tests are based on quality controls based on positive and negative controls. Positive control equivalent to >15 mg/dL (sesuaikan dengan merek reagen yang digunakan merk GLORY). Typically, CRP is present in very small amounts in plasma (about 0.6 mg/dL) in healthy individuals. However, its concentration may increase in the blood in response to inflammation or tissue damage (Shankar et al., 2023). A positive or reactive result indicates that the CRP level is greater than 15 mg/dL, while a negative or non-reactive result indicates that the level is less than 15 mg/dL. The positive control value corresponds to 15 mg/dL or above, depending on the type of CRP product used.

Other interpretation criteria are as follows: Less than 0.3 mg/dL: normal (level seen in most healthy adults). 0.3 to 1.0 mg/dl: normal or minor increase (may be seen in obesity, pregnancy, depression, diabetes, common flu, gingivitis, periodontitis, low-movement lifestyle, smoking, and genetic polymorphism). 1.0 to 10.0 mg/dL: moderate increase (systemic transmissions such as RA, SLE, or other autoimmune diseases; terrorism; myocardial infarction; pancreatitis; bronchitis). More than 10,0 mg/l: significant increase (acute bacterial infection, viral infections, systemic vasculitis, major trauma)(Patel, 2023).

Pregnant mothers are said to have inflammation due to ruptured wounds and pain during childbirth. Characteristics of the presence of inflammation are characterized by five characteristics, such as heat, redness, swelling, loss of flavor, and pain. The postnatal mother will have a birth trauma. The wound has a Damage Association Molecule Pattern (DAMP) of the damaged tissue or cell. DAMP will be recognized by the TLR (M.J.Portou et al., 2015; Geng et al., 2021), which will subsequently induce the host cell to release pro-inflammatory cytokines (Muin et al., 2021). C-reactive protein (CRP) triggers the activation of the complement system and enhances the process of phagocytosis by macrophages (Haapasalo & Meri, 2019; Miller & Stevens, 2021). CRP can attach to cells that are breaking down as well as cell debris. Additionally, CRP triggers the activation of the complement system via the classical C1q pathway (Jialal., 2023).

DAMP has the ability to activate molecular structures called inflammasomes, especially in monocytes and macrophages, as well as other cell types like neutrophils and even endothelial cells. This activation quickly triggers the ripening and release of pro-inflammatory cytokines IL-1 β and IL-18 into the extracellular environment (Gong et al., 2020). These cytokines are a major trigger in the initial process of the inflammatory cascade (Caballero-Herrero et al., 2023).

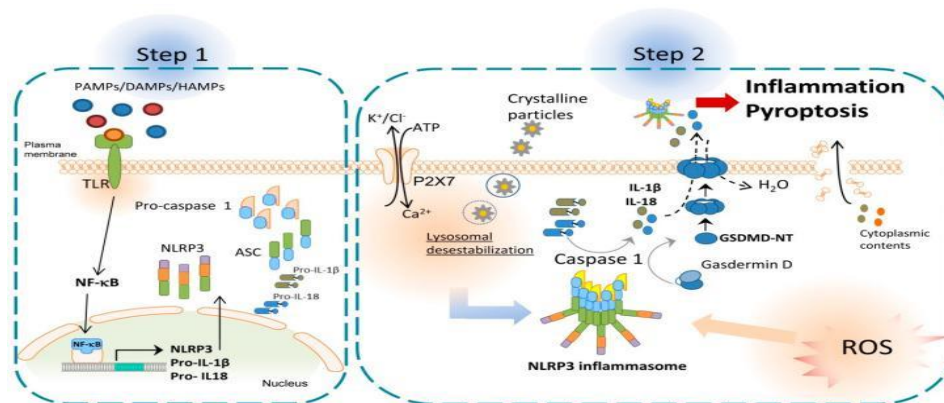


Figure 1. DAMP can activate NLRP3 inflammasome (Pitharouli et al., 2021)

NLRP3 inflammasoma activation begins with stimulation of TLR receptors by pathogen-related molecular patterns (PAMPs), host-damaged molecule pattern (DAMPs) and homeostasis modification processes. (HAMP) (Gong et al., 2020). The first step allows the translocation of NK- κ B into the nucleus of the cell, which increases the transcription of the inflammasome components, pro-IL-1 β , and pro-IL-18 (Quansah et al., 2023). The second step requires additional signals such as activation of P2X7 by ATP, lysosomal destabilization by crystal particles, or ROS production to induce oligomerization of inflammasoma NLRP3 and caspase activation 1. Caspase 1 then converts pro-IL-1 β and Pro-IL-18 into active cytokines as well as divides gasdermine D to form membrane pores. These pores trigger pyroptosis and inflammation by releasing pro-inflammatory cytokines and NLRP3 inflammasoma complexes from cells (Pitharouli et al., 2021)

CONCLUSION

Based on a study of 30 samples of normal postpartum patients, it can be concluded that the C-reactive protein examination showed that 26 samples (86,7%) showed positive results and 4 samples (13,3%) showed negative results. This test is based on the return time of one or two days for the postnatal mother. Interventions guided by CRP monitoring can significantly improve postpartum care. Some examples of these interventions include early detection of infection, management of preeclampsia, mental health interventions, monitoring and management of gestational diabetes, and lifestyle modification.

C-Reactive Protein (CRP) levels in normal postpartum mothers can provide important insights into the inflammatory status and the possibility of postpartum infection. CRP is a commonly used biomarker to assess the level of inflammation in the body. If CRP levels increase after delivery, this may indicate the presence of infection or inflammatory complications. Therefore, monitoring CRP levels can help in early detection of problems that may require further medical attention, such as endometritis infection or other complications. Limitations of this study, such as the small sample size; future studies should involve a larger sample size to increase the generalizability of the results and ensure that the findings can be applied to a wider population. Suggestions for future research based on the findings of this study, namely the use of additional biomarkers and combining CRP with other biomarkers to provide a more comprehensive picture of the inflammatory status and health of postpartum mothers.

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