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Differences of Neutrophil-Lymphocyte Ratio and Wound Healing of Post Caesarean Section in Patients Given Transversus Abdominis Plane Block Analgesia versus Post-Operative Wound Infiltration, A Randomized Controlled Trial

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Abstract:- Transversus abdominis plane (TAP) block and local infiltration anesthesia in post-operative wound have been reported to be an effective analgesia methods for post-caesarean section patients. There is still no study that investigate the influence of these analgesic methods toward post-operative wound healing. Nevertheless, recent studies showed that neutrophil-lymphocyte ratio (NLR) could be a discriminative marker to assess the severity of stress and inflammation, and to predict the post-operative wound healing. This randomized controlled trial (RCT) aims to compare the effects of TAP block and post-operative wound infiltration methods toward post-operative wound healing outcome and NLR. This RCT included 30 pregnant women that underwent Caesarean Section with PS ASA 1-2. Participants were allocated into 3 groups based on the analgesia methods: TAP (n=10), post-operative wound infiltration (n=10), and control group. Spinal anesthesia was performed in all study participants. Post-operative assessment was performed 72 hours after the operation using BWAT scale for the assessment of wound healing and complete blood count analysis for the assessment of NLR. The collected data were analyzed statistically using SPSS, with significance of ≤0.05. A statistically significant difference of post-operative woud healing (measured using BWAT scale), NLR, and delta NLR were demonstrated among the study groups (p < 0.001). Compared to the post-operative wound infiltration group and the control group, TAP blocking group showed the best post-operative wound healing improvement (showed by the lowest BWAT scale). Alongside with the wound healing improvement, the best outcome for 72-hour post-operative NLR and delta NLR were also showed in TAP blocking group. This study also demonstrated a strong correlation of delta NLR and wound healing improvement in post caesarean section patients. TAP blocking method improved post-caesarean section wound healing outcome and reduce NLR better than wound infiltration method and standard analgesia alone.

Keywords:- *Transversus abdominis plane block, post-operative wound infiltration, neutrophil to lymphocyte ratio, post-operative wound healing, BWAT scale.*

I. INTRODUCTION

Caesarean section is the most frequent major operation that performed worldwide. Lancet registry showed a significant increase of caesarean section number globally, from 12.1% in 2000 to 21.1% in 2015 [1]. Wound healing is one of the important factors in post-caesarean section recovery. The combination of vascular, cellular, and chemical responses as mediators in wound area becomes the integrated components in the wound healing process. Wound healing process consists of 4 phases: hemostasis, inflammation, proliferation, and maturation [2]. Many factors could affect wound healing process, including post-operative pain, that is widely investigated recently.

Post-caesarean section pain management still becomes a major concern until now, that 79% of women experienced pain in the incision site after the caesarean section. Pain severity post- caesarean section is in the 9th rank of 179 operation procedures, and 7% of post-caesarean section women experienced moderate to severe pain [3]. As responses to pain stimuli, type C nerve fibers release pain neuropeptides (substance P and neurokinin A) that activate leukocytes and the other immunoactive properties such as glial cells, to release proinflammatory cytokines. These proinflammatory cytokines were proved to increase the

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pain signals and stress responses [4,5]. These stress responses are complex and are intercorrelated by neuroendocrine, inflammation, and nociceptive phenomena. During this stressful condition, glucocorticoid (cortisol) is released by the adrenal gland and was proved to affect the immunity system by suppressing the proliferation and the differentiation of cells and by reducing genes transcriptions and adhesion molecules that are essential for cells migration. In the presence of cortisol, T cells become less responsive to signals from interleukin-1 (IL-1), whereas IL-1 produces growth factors to facilitate the proliferation of T cells [5,6]. McBeth proved that there was no inhibition in the production of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and corticosteroid during painful condition [7]. Excessive cortisol and catecholamine as the stress response could negatively influence the wound healing, because of: immunity impairments, tissue hypoxia-induced vasoconstriction, hyperglycemia, and macrophages suppression. Therefore, adequate analgesia treatments after caesarean section could improve post-operative wound healing by preventing stress responses that are elicited by the pain and all of the negative effects to wound healing [5,8].

Ketorolac is one of the non-steroidal anti-inflammatory drug (NSAID) that is widely used for post-caesarean section pain management because of the strong analgesic effect that is equal to opioid analgesia. Tramadol works centrally to overcome moderate-to-severe pain. It has a moderate affinity to μ receptor, and weak affinity to opioid receptor κ and δ [9]. The combination of ketorolac dan tramadol is frequently used as the standard therapy for post-operative pain, including post-caesarean section. Nevertheless, some studies showed that this combination was still not effective as post-operative pain management [10,11].

Peripheral nerve block proved to be one of the post-operative pain management alternatives. It could improve the analgesic effects and reduced the opioid use thus also reduced the side effects elicited by the opioid [3,12,13]. According to the concept of "Enhanced recovery after caesarean", the recommended peripheral nerve blocks are TAP block, wound infiltration, and quadratus lumborum (QL) block [12,13]. Numerous studies demonstrated that local analgesia using wound infiltration method could improve post-operative wound healing through the adequate inhibition of pain and through its anti-bacterial effects [14,15,16]. However, there is still no study that compares the effects of TAP block and wound infiltration method toward post-operative wound healing .

Clinically, the improvement of the post-operative wound healing could be assessed using the Bates-Jensen Wound Assesment Tool (BWAT) scale. BWAT scale has long been used internationally to assess the wound healing in various wound types, including post-operative wound. BWAT scale had good validity and reliability to assess the wound healing improvement, and could be an objective instrument to measure the wound healing improvement [17].

Inflammation is an essential factor in the wound healing process. Physiologic inflammation involved the circulating polymorphonuclear cells, adherence, diapedesis, chemotaxis, phagocytosis, and destruction of invading bacteria. This process is regulated by inflammation and anti-inflammation mediators. The systemic inflammatory reaction leads to the endothelial destruction, microvascular dysfunction, tissue oxygenation impairment, and organic trauma, while excessive anti-inflammatory reaction leads to allergy and immunosuppression [2,18]. The inflammatory biomarkers had been well observed, such as C- reactive protein (CRP). But in the implementation, the analysis of those biomarkers are limited due to facility and funding circumstances. Therefore, researches were conducted to find the reproducible and cheap yet reliable biomarker to be implemented. One of the inflammatory biomarker that meets those criteria is NLR. This parameter had been proved to be correlated with cardiovascular mortality, worse prognosis in some cancer types, inflammation or pathologic infection such as pediatric appendicitis, and post-operative complications [19]. Recently, NLR is introduced as the potential biomarker to assess inflammation and to predict post-operative wound healing progression [19,20].

II. METHODS

This research is a prospective single-blind randomized controlled trial (RCT) research model in post-operative caesarean section patient with spinal anesthesia with TAP block , wound infiltration and control (standard analgesia) intervention with wound healing and post-operative NLR as outcomes. This research already approved by Dr. Soetomo Hospital ethical committee.

This RCT included women patients underwent caesarean section in Dr. Soetomo hospital from February to April 2020. The inclusion criterion in this rct were 18 – 40 age years old patients underwent caesarean section with spinal anesthesia and PS ASA 1- 2, pfanennesnstiel incision, and willing to sign informed consent, while the exclusion criteria is patients with a history of anesthesia drug allergy; significant heart, liver or renal failure; impending eclampsia or eclampsia, HELLP syndrome; diabetes mellitus; IUFD, premature rupture of membranes with infection sign, operative and post-operative massive bleeding, prolonged blood coagulation, local wound infection; psychiatric disorder; immunocompromised (HIV) patients and patients with BMI more than 40. The drop out criterion in this RCT was anesthesia method changes to general anesthesia in prolonged (more than 3 hours) operation; local anesthetic systemic toxicity, and patients withdrawal from RCT.

Data was collected with consecutive sampling method, the sample would be randomized, single-blinded and assigned into 3 groups, control group (ketorolac and tramadol as analgesia), TAP block group (TAP and standard analgesia), wound infiltration group (wound infiltration and standard analgesia).

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Pre-operative visitation would be done to asses comorbidities, pain scale with Wong-Baker Faces Scale (WBFS) and standard laboratory examination such as complete blood count, albumin level, blood coagulation and other indicated examination, explain research procedure and obtain informed consent. Patients would be monitored with ASA standard and received 10 ml kg^{-1} BW^{-1} pre-spinal anesthesia induction. Spinal anesthesia would be done with 26G quincke spinal needle in left lateral decubitus (LLD) position in paramedian lumbal 3-4 vertebral space with bevel parallelled with a sagittal plane to prevent a larger dural tear. Local anesthesia (1,4 ml lidocaine (Lidodex$^{TM)}$ 5%) then injected in cephalad position with 1 ml per second rate.

Before the operation was done, wound infiltration group would received 10 ml local anesthetic (Ropivacaine 0,2%) infiltration with subcutaneous injection in both upper and lower side of the incision performed by obstetrician after fascia closure above rectus muscle and before skin closure. TAP block group would receive TAP block performed by regional anesthesia consultant anesthesiologist with USG guiding. USG used in this RCT is Sonosite© linear probe (5-12 MHz) with 4-6 cm depth. USG probe USG was placed in mid axillary line between lower costae and iliac crest to evaluate the anatomic structure, stimuplex needle then inserted within USG probe view to reach space between internus obliquus and transversus abdominis muscle, then 1ml NaCl 0,9% would be injected to asses needle placement by confirming hypoechoic space between obliquus internus and transversus abdominis muscle (transversus abdominis plane), then 20 ml ropivacaine 0,2% would be injected in both side. Control group would receive standard analgesia, 30 mg ketorolac and 75 mg tramadol intravenous injection every 8 hours. All patients with $\geq$ 4 pain scale would receive 50 mcg fentanyl intravenous injection as rescue analgesia.

Pain scale would be evaluated with WBFS after 48 hours in all groups. Wound healing would be evaluated after 72 hours with BWAT scale, this scale consists of 13 items, wound width, depth, edge, undermining and tunnelling processes, necrotic tissue type and amount, exudate type and amount, surrounding skin discoloration, tissue edema, peripheral tissue induration, tissue granulation and ephitelialization. Venous blood would be collected after 72 hours post-operative with aseptic method within EDTA tube, tested for complete blood count and differential count using Sysmex XN-1000 in Clinical pathology laboratory of Dr.Soetomo genera hospital and calculated to obtained NLR. BWAT scale and NLR were analyzed with SPSS. $P< 0.05$ was considered significant.

III. RESULTS

Thirty patients were enrolled in this RCT. All patients then randomized and 10 patients would be assigned each control, wound infiltration and TAP block group. We found no significant differences within patient demography (Table.1) such as age, BMI, parity, gestational age, operation type, caesarean section indication, comorbidities and PS ASA ($p > 0.05$). Pre-operative laboratory examination also showed no significant differences ($p > 0.05$).

Characteristic	Group			p value
	TAP Block	Wound Infiltration	Control	
	n = 10	n = 10	n = 10	
Age				0.571*
20-30	2	1	1	
31-35	7	5	7	
>35	1	4	2	
BMI				0.749*
$\leq$ 30	9	8	9	
> 30	1	2	1	
Parity				0.315*
Primigravida	2	0	2	
Multigravida	8	10	8	
Gestational Age				0.875*
$\leq$ 37 weeks	5	6	5	
> 37 weeks	5	4	5	

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Operation type				0.383*
Elective	3	1	1	
Cito / Emergency	7	9	9	
Caesarean Section Indication				0.061*
Mother indication	5	6	2	
Fetal indication	5	4	8	
Comorbidities				0.865*
Hyperthyroidism	2	1	0	
Hypertension in pregnancy	4	4	4	
Obesity	1	2	1	
No comorbidities	3	3	5	
PS ASA				0.328*
ASA 1	2	0	2	
ASA 2	8	10	8	

Kruskal Wallis Test
*Annova test
Significant if p < 0,05

Table 1:- Study Sample Characteristics Demography in TAP, Wound Infiltration and control Group

Laboratory value	TAP Block	Wound Infiltration	Control	p value
Hb	11,3 (9,6-12,7)	11,15 (8,5-13)	10,7 (8,5-13)	0,523#
Leukocyte	10,31 ± 1,92	10,40 ± 2,03	10,65 ± 1,41	0,907*
Platelet	266,60 + 39,60	266 + 45,08	299,70 + 43,11	0,149*
Albumin	3,15 (3,0-3,4)	3,15 (3,1-3,6)	3,35 (3,1-3,7)	0,373#
Random blood glucose	110 ± 21,64	103,7 ± 33,51	110,60 ± 19,26	0,801*

Kruskal Wallis Test
*Annova test
Significant if p < 0,05

Table 2:- Pre-Operative Laboratory Value Characteristic

WBFS	TAP Block	Wound Infiltration	Control	p value
Pre-Op	0,5 (0-1,0)	0,5 (0-2,0)	1,0 (0-2,0)	0,631*
48 hours Post-Op	2,5 (1-3)	3 (3-4)	3 (3-5)	0,004*

*Kruskal-Wallis test, Significant if p < 0,05

Table 3:- Pre-operative and 48 hours WBFS pain scale

No significant difference was found within each group's pre-operative WBFS pain scale (p = 0.631), while significant difference was found in 48 hours postoperative pain scale (p = 0.004) which TAP block group demonstrate lowest pain scale in all groups. Significant BWAT scale difference was found, which TAP block group demonstrate better wound healing and lower score than wound infiltration and control group (p < 0.001) (table 4).

BWAT Scale	TAP Block	Wound Infiltration	Control	p value
72 Hours Post-Op	14 (14-23)	22 (20-24)	30 (29-35)	< 0,001*

* Kruskal Wallis Test, Significant if p < 0,05

Table 4:- Post-Operative BWAT scale

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Pre-operative NLR were similar between each group (p = 0,309), while we found significant in 72 hours post operative NLR (p < 0.001, table 5). Table 5 also demonstrate significant changes in pre-operative NLR {4,38 (2,13-29,6)} and 72 hours post-operative NLR (2,93 ± 0,76) in TAP group (p = 0.022). While, no significant changes were observed in pre-operative and 72 hours post-operative NLR of control and wound infiltration group (p > 0.05), which demonstrate elevation in 72 hours post operative NLR.

Pre and post-operative NLR changes (delta Δ) (%) demonstrate significant differences between 3 groups (p = 0.002), while TAP block demontrated lowest delta NLR (table 7). A significant correlation was found between wound healing according to post-operative BWAT scale and delta NLR (p = 0.009), where every delta NLR increment (%) would be followed by BWAT scale increment, vice versa (picture 1).

NLR	TAP Block	Wound Infiltration	control	p value
Pre-Op	4,38 (2,13-29,6)	6,12 (3,5-11,5)	4,86 (3,02-26,77)	0,309#
72 hours Post Op	2,93 ± 0,76	7,77 ± 0,78	14,14 ± 3,16	< 0,001*

*Annova test
Kruskal Wallis test
Significant if p < 0,05

Table 5:- Delta Pre and Post-Operative Neutrophil and Lymphocyte Ratio (NLR)

Group	Neutrophil and Lymphocyte Ratio		p value
	Pre Operative	72 Hours Post Operative	
TAP Block	6,65 ± 8,18	2,93 ± 0,76	0,022*
Wound Infiltration	6,72 ± 2,61	7,77 ± 0,78	0,314*
control	9,11 ± 7,59	14,14 ± 3,16	0,093*

*Wilcoxon Signed Ranks Test, Significant if p < 0,05

Table 6:- Pre and 72 Hours Post-Operative Neutrophil And Lymphocyte Ratio (NLR)

	TAP Block	Wound Infiltration	Control	p value
Delta NLR (%)	-24,91 (-84,45-37,35)	18,71 (-27,44-157,14)	210,83 (-58,2 – 275)	0,002*

*Kruskal Wallis Test, Significant if p < 0,05

Table 7:- Delta Pre and Post-Operative Neutrophil And Lymphocyte Ratio (NLR)(%)

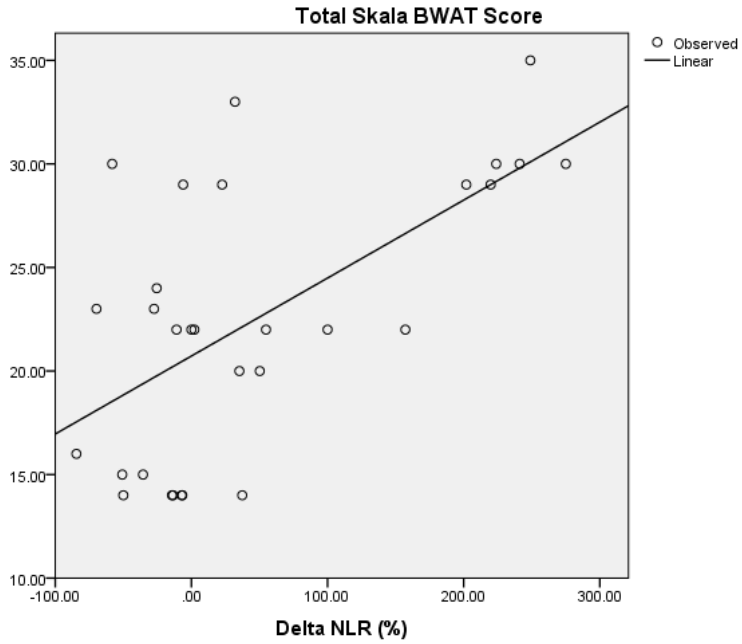

Fig 1:- Pre and Post-Operative Bates-Jensen Wound Assessment Tool (BWAT) scale and Neutrophil And Lymphocyte Ratio (NLR) correlation (p = 0.009)

IV. DISCUSSION

Basic characteristics in the study population and laboratory values before the caesarean section showed that there was no significant difference in the demographic distribution among the 3 groups, so this RCT provided good randomization that no bias could interfere the results, because the characteristics of the 3 study groups were homogenous and could be compared equally.

This study showed that TAP block significantly improves wound healing better than wound infiltration and standard analgesia alone. This result is strongly correlated with the lower pain scale 48-hours after the caesarean section in TAP block group, compared with the wound infiltration group and the control group. This results was in accordance with the study from Mc Guire et al that prospectively investigated the correlation of pain and wound healing in 17 patients after gastric bypass surgery patients for 5 weeks period, in which every patients were incised 2mm long. This study showed a significant correlation between pain and wound healing. Patients with a higher pain scale 48 hours after the operation was significantly correlated with the attenuation of post-operative wound healing (*log rank test*, p 0,023).

TAP block had been proven as the effective method to reduce post-operative pain and to suppress the opioid use after caesarean section and lower abdomen operation [21,22,23,24]. The study from Staker in 100 women who underwent caesarean section showed that TAP block significantly reduces the post-operative pain scale at rest and during activity [21]. Meanwhile, a study from Christrijogo in Dr Soetomo General Hospital in 30 patients who underwent lower abdomen operation showed that patients that were given TAP block significantly had the lower pain scale compared to the control group at 24 hours after the operation [22]. Yu et al conducted a meta-analysis in 4 studies to investigate the effectivity of TAP block compared to wound infiltration in adult patients that underwent various lower abdomen operation, and it is demonstrated that post-operative pain scale reductions were shown at 24 hours after the operation [23]. Similar with Yu et al (2014), a meta-analysis from Guo et al (2015) analyzed 9 studies that compare the TAP block and wound infiltration method, but with more heterogenous patients characteristics (children and adults, including the giving birth women) who underwent an abdominal operation (laparoscopy, laparotomy, and caesarean section), and proved that post-operative pain scales were significantly lower in TAP block group at 8 and 24 hours after the operation [25].

Pain is a physiologic consequence of the surgical incision; however, inadequate post-operative pain management caused negative post-operative effects for the patients, such as stress, haemodynamic disturbance, respiratory disturbance, urine retention, ileus, and etcetera. These conditions impair the wound healing process. Post-operative pain is a stressor that induces the metabolic stress response (MSR) that leads to the attenuation of post-operative wound healing process [4,6]. Pain and stress responses could impair the wound healing through various ways. As the continuous pain responses, type C nerve fibers release neuropeptides (substance P and neurokinin A) which then will activate leukocytes and the other immunoactive properties (such as glial cells) that react by releasing pro-inflammatory cytokines. Pro-inflammatory cytokines amplify the pain signals and stress responses to the body, so if the pain is not treated, this vicious cycle will continue and leads to the impairment of wound healing process [5,26].

In the hypothalamus, stress signals caused by pain activates the production of CRH which increases the production of ACTH from the anterior pituitary gland. ACTH stimulates the adrenal gland to produce glucocorticoid hormones (mainly cortisol) from the adrenal cortex and catecholamines from the adrenal medulla. Glucocorticoid hormones affect the immune system by suppressing cell proliferation and differentiation, suppressing gene transcriptions, and reducing the release of cellular adhesion molecules. The overproduction of CRH, ACTH, and corticosteroid was documented in continuous stress condition due to pain [7]. The overproduction of cortisol and catecholamines that was caused by the stress response could significantly impair the wound healing process because of the impairment of immunity system and tissue hypoxia [4,5].

Moreover, in a state of pain, there was an increase of β endorphin secreted by the pituitary gland which suppresses macrophages, so that macrophages activities stimulated by IFN γ are reduced, thus the activity of cytokines released by macrophages such as TNF α, IL-1, IL-6, IL- 8, TGFβ will decrease. The decrease of these growth factors leads to the inhibition of wound healing process. The increase of cortisol hormone which is induced by pain will also inhibit the other growth factors such as IL-1 that stimulates cells to develop procollagenase in the formation of collagenase [5,26].

Analgesia treatment using TAP block was proved to reduce pain effectively post-caesarean section, so it could cease the wound healing impairment process caused by the stress responses which were induced by pain. The improvement of post-operative wound healing by TAP block analgesia was measured with the better outcome of BWAT scale in TAP block group compared to wound infiltration group and standard analgesia alone. Our results were alongside with the study from Mc Donnel et al which stated that the post-caesarean section pain was elicited by the incision wound in the anterior abdomen area [3]. Nerves that innervates skin, muscle, parietal peritoneum and anterior wall of the abdomen were originated from T8-L1 and passing through the plane between transverse abdominal muscle and internal oblique muscle which could be blocked by TAP block [27].

Our study showed that there was no significant difference in the mean of NLR before caesarean section in the 3 study groups (p > 0,05), so it could be concluded that the significant differences of post-operative NLR among the 3 study groups were not caused by the baseline NLR before the caesarean section. Meanwhile, NLR at 72 hours after the operation showed a significant difference among the 3 groups (p > 0,05). There were also significant differences in the delta NLR among the 3 study groups, with the greatest NLR reduction at 72-hours post caesarean section was demonstrated by TAP block group compared to wound infiltration group and control group.

Dilektasli observed that NLR is a fast, simple, and reliable method to evaluate stress and inflammation severities. This study showed significant differences in the mean of pain scales at 48 hours post-operatively, and TAP block group had the lowest post-operative pain scale. Therefore we assumed that the greatest NLR reaction by TAP block was because of its greatest pain reduction effects that caused the reduction of the stress response and inflammation [28]. Canbolat et al also showed similar results in the correlation of post-operation pain and NLR in patients post knee and thigh arthroplasties, in which a significant correlation between the post-operative pain scale at 48 hours and post-operative NLR value was demonstrated (p = 0,031) [29]. Zahorec stated that the general physiologic responses of leukocytes in the circulation towards stress was by increasing neutrophil production (neutrophilia) and reducing lymphocytes production (lymphopenia), so it caused the increase of NLR [30]. Soon dan Acton investigated that pain could cause a stress response in the body [4]. Thus, the higher NLR values in wound infiltration group and control group were caused by the higher pain scales that induce the stress responses, neutrophilia, and lymphopenia.

Our study showed a strong correlation between delta NLR and BWAT scale at 72 hours after the caesarean section. Each increase of the delta NLR was also followed by the increase of BWAT scale. Maruyama et al also showed a significant correlation between NLR value and post-operative wound healing improvement in head and neck surgery. There were significant differences of the wound healing failure in patients with NLR < 3,5 compared to those with NLR $\geq$ 3,5 so that a cutoff point of 3.5 with the sensitivity of 82.4% and specificity of 48.3 were obtained [31]. Kahramanoglu also observed that NLR value was correlated with the infection of post-hysterectomi wounds. Patients with post-operative wound infection after the hysterectomies had a significantly higher NLR value compared to those who without post-operative wound infection [32]. Meanwhile, retrospective study from Kondratiuk in 133 patients with gunshot wounds showed that there was a correlation between the NLR value and the wound healing duration, in which the higher NLR value was correlated with the longer wound healing duration, with the cutoff point of 2.49 (sensitivity of 82% and specificity of 58%) [33]. Vatankhah also reported that NLR value > 4,19 was correlated with the worse wound healing process in diabetic foot patients [34]. Bolat et al showed that NLR value in patients who developed post-operative wound complications in penis prosthetic implant operation was greater compared to those who did not develop the post-operative wound complications [35].

According to the researchers, the correlation between postoperative NLR and wound healing (measured by BWAT scale) was because of the essential roles of neutrophils and lymphocytes in the production of pro-and anti-inflammatory cytokines in the process of postoperative wound healing. Surgical incisions were traumatic stimuli that activated neuroendocrine responses and local and systemic inflammatory responses, and surgical trauma could cause acute phase responses. The Acute phase response is useful for controlling the infection and tissue damage and initiating the healing process. Neutrophils play an integral role in the initial phase of inflammation, specifically in the phagocytosis process to destroy and eliminate bacteria, foreign particles and damaged tissue. During the period of 72 hours after the operation, there were neutrophils migration from the wound matrix and monocytes differentiation to tissue macrophages that could phagocyte the neutrophils and debris, and also could activate the lymphocytes. The lymphocytes involvement at 72 hours after an injury caused the transition from proinflammatory state to anti-inflammatory state; it also released the growth factors that activated proliferation phase in wound healing process. This process causes the neutrophil value to decrease 72 hours postoperatively and followed by the increase in lymphocyte values so that a low NLR value will be obtained as the results of the resolution of inflammation and the beginning of the proliferative phase in the improvement of wound healing [2,18,36].

- *Study limitations*

Thorough assessments of confounding factor to the wound healing, such as nutritional status before the caesarean section were not performed in this study. Despite that limitation, anthropometry assessments (weight, height, body mass index), serum albumin and hemoglobin measurement were performed preoperatively, to reduce the potential bias that could be caused by the confounding factor, and there were no significant differences in the preoperative weight, height, boy mass index, serum albumin level, and hemoglobin concentration among the 3 study groups.

This study assessed the wound healing improvement (measured with BWAT scale) at 72 hours after the caesarean section which theoretically at the proliferative phase of the wound healing, but did not assess until the completion of wound healing process, because of the time limitation and also the difficulties in the long-term follow-up assessments which could take up to 2 years until the wound healing completion. Thus, further researches are needed to investigate the post-operative wound healing until the completion of wound healing process so that could conclude the long-term effects of TAP block compared to the wound infiltration and standard analgesia alone in the wound healing process.

V. CONCLUSION

This study demonstrated differences in wound healing according to BWAT scale between post caesarean patients who received standard analgesia, wound infiltration and TAP block. TAP block also significantly reduce post-operative NLR compared with standard analgesic and wound infiltration. A significant correlation between wound healing (BWAT scale) and delta NLR was also demonstrated in this study. Multimodal analgesia with peripheral nerve block such as TAP block is recommended in post-operative caesarean section patient which evidently reduce post-operative pain, promote wound healing and reduce post-operative NLR.

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