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Neuroendocrine and Inflammatory Responses in Laparoscopic Versus Abdominal Hysterectomy: Clinical Trial

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Abstract

Women most often have hysterectomy, a significant gynecological procedure that involves the removal of the uterus and sometimes other surrounding tissues such as the cervix, ovaries, and fallopian tubes (salpingectomy). Abdominal hysterectomy (AH) and vaginal hysterectomy were the two main methods used in the past for hysterectomy. Laparoscopic surgery is an evolving new surgical technology, and as regard to hysterectomy, it appeared to have a favorable clinical outcome than that of conventional open surgery. To compare the effect of surgical trauma in laparoscopic hysterectomy versus abdominal hysterectomy; through measuring the levels of inflammatory mediators "IL-6 & CRP" and neuroendocrine mediators "cortisol". Twenty-four patients with no major medical disease were randomly assigned to undergo laparoscopic) n = 12) or abdominal hysterectomy (n = 12). Venous blood samples were collected and we measured the levels of interleukin-6 (IL-6), CRP and cortisol at the time before anesthesia in the ward, 10 minutes after skin incision, at the end of peritoneum closure or port removal in laparoscopic hysterectomy, and at 1 h and 24 h after operation. There was no statistically significant difference between laparoscopic hysterectomy and abdominal hysterectomy regarding interleukin-6 (IL-6), CRP, and cortisol levels ($P < 0.05$). There was no statistically significant difference between laparoscopic hysterectomy and abdominal hysterectomy with regard to anesthesia time or surgery time ($P < 0.05$). Hospital stay was shorter in the laparoscopic hysterectomy group but this difference was not statistically significant ($P < 0.05$). Inflammatory response after total abdominal hysterectomy "TAH" and total laparoscopic hysterectomy "TLH" is equal as shown by measuring IL-6, CRP & Cortisol. Teaching might have impact on advantages of laparoscopic surgeries in comparison to open surgeries. Simulation training might help speed teaching curve and improve performance and consequently patients' outcomes.

Keywords: Neuroendocrine; Laparoscopic; Abdominal; Hysterectomy; Interleukine-6.

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1. Introduction

Hysterectomy is a surgical procedure that excises the uterus and may also include the surgical removal of the cervix, ovaries (oophorectomy), fallopian tubes (salpingectomy), and any other adjacent tissues. It is the most often done major gynecological operation in women. Around thirty percent of women by age of 60 and 590,000 surgeries performed yearly in the USA have hysterectomy for benign disorders. Such conditions include uterine leiomyoma, prolapse of pelvic organs, and menorrhagia [1-2]. The conventional methods for hysterectomy were laparotomy, known as abdominal hysterectomy (AH), or vaginal procedures [1]. The laparoscopic technique for hysterectomy has advanced dramatically throughout the last two decades. Kurt Semm pioneered the use of laparoscopic aid in complex vaginal hysterectomy in 1984, which was subsequently evolved into laparoscopically aided vaginal hysterectomy as outlined by Harry Reich [3-4]. Laparoscopic hysterectomy is linked to reduced hospital stay, faster healing, and a lower incidence of post-operative infections in comparison to abdominal hysterectomy. A comparative analysis suggests that laparoscopic hysterectomy is more favorable than abdominal hysterectomy [1-5].

The systemic reaction to surgical damage, known as surgical stress, is marked by the stimulation of the sympathetic nervous system, endocrine reactions, and immunological and hematological alterations [6-7]. The surgical stress response occurs due to direct and indirect injuries during surgery, where greater degrees of tissue injury will lead to higher levels of inflammatory mediators and cytokine release; this will then influence postoperative convalescence and recovery [8-9]. Quantification of plasma

concentrations of specific proteins and enzymes associated with tissue damage, such as creatine phospho-kinase (CPK), C reactive protein (CRP), lactic dehydrogenase (LDH), CA 125, tumor necrosis factor-a (TNF-α), and interleukin 6 (IL-6), can be used to assess the severity of operative trauma [8-9]. In addition to enhancing recovery after surgery (ERAS), the laparoscopic technique for hysterectomy represents a paradigm change in perioperative care, leading to substantial enhancements in clinical outcomes and cost savings [10]. By assessing the amount of inflammatory mediators "IL-6 & CRP" and neuroendocrine mediators "cortisol", this research aims to evaluate the impact of surgical trauma in laparoscopic hysterectomy versus abdominal hysterectomy.

2. Materials and Methods

The study was conducted at Ain-Shams University Maternity Hospital, Egypt after receiving approval from hospital's ethical committee, and informed, written consent was obtained from all patients. Twenty four patients who were scheduled for elective total hysterectomy for nonmalignant disease were studied preoperatively and for 24 hours after their operations. Patients were randomly allocated to receive either total abdominal hysterectomy (TAH) or total laparoscopic hysterectomy (TLH) for their benign disease. Patients with BMI > 35 Kg/m ^{2} or with major medical disorders were excluded from study. Patients divided into two groups; laparoscopic(n = 12) or abdominal hysterectomy group (n = 12). Preoperatively, all cases received antibiotic prophylaxis with 1 g of 3rd generation cephalosporin (Cefotaxime®, EIPICO/Egypt) intravenously. All cases placed under general anesthesia along with performing endotracheal intubation. Anesthesia induced with IV bolus of thiopental sodium (5 mg/kg) or propofol (2 mg/kg), and tracheal intubation facilitated with IV atracurium besylate (Tracium®, GSK/Egypt, 0.08 mg/kg). Anesthesia maintained with inhalation of isoflurane in 40% O2 in air and cases ventilated to maintain an end tidal PaCO2 of 35-45 mmHg.

Venous blood samples were collected from each patient for measuring levels of interleukin-6 (IL-6), CRP and cortisol as a primary outcome at following times: a baseline sample before surgery (T0), 10 minutes after skin incision (T1), at the end of peritoneum closure or after removal of laparoscopic ports in laparoscopic hysterectomy (T2), 1 h after the operation (T3) and 24 h after the operation (T4). The IL-6 in serum was analyzed using a commercially available enzyme-linked immunosorbent assay (ELISA) method (IL-6 Quantikan kit; R & D systems, Minneapolis, MN, USA) with a detection limit of 0.3 pg/ml. Serum cortisol was determined by immune-enzyme assay (Roche cobas® e 601 & e 602, GmbH, Mannheim) with a sensitivity of 0.1 µg/dl (normal reference range: 0.054-63.4 µg/dl). The C-reactive protein (CRP) measured by an immunoturbidimetric assay (Roche Diagnostics, IN, USA). The detection limit of this assay was 0.425 mg/L. Duration of anesthesia "from time of induction of general anesthesia until patient is fully conscious", duration of surgery "from time of skin incision till the time of skin closure", duration of hospital stay, major complications (major hemorrhage, bowel injury, ureteric injury etc..) or minor complications (minor hemorrhage, fever, hematoma etc..) were measured as a secondary outcome.

Statistical analysis was done using Data were analyzed using IBM© SPSS© Statistics version 26 (IBM© Corp., Armonk, NY) and MedCalc® Statistical Software version 20 *(MedCalc Software Ltd, Ostend, Belgium;https://www.medcalc.org; 2021).* Categorical variables are presented as counts and percentages and intergroup differences are compared using the Fisher's exact test. Continuous numerical variables are presented as mean and standard deviation and intergroup differences are compared with the independent-samples t-test. Serial measurement analysis is used to calculate summary measures for IL.6, CRP and cortisol using the methods described by *Mathews et al., 1990*. Area under the time-VAS curve (AUC), time-weighted average (TWA) and minimum and maximum values are calculated and compared between groups using unpaired t-test. Repeated measures analysis of variance (ANOVA) is used to examine between-group and within-group effects as regards the change in IL-6, CRP or cortisol. Correlation between IL-6 and CRP was analyzed using Pearson's correlation coefficient. P-values <0.05 are considered statistically significant.

3. Results and discussion

3.1. Results

There was no difference between two groups with respect to age, weight, operation time and duration of anesthesia. Hospital stay was shorter in TLH group than TAH group, but this difference was not statistically significant ($p < 0.05$). There was no statistically significant difference between laparoscopic hysterectomy and abdominal hysterectomy regarding interleukin-6 (IL-6), CRP, and cortisol levels. The median IL-6 level for TAH group (range) was 138.5 (86.3 - 211.6) pg/ml, 78.8 (50.6 - 132.7) pg/ml and 98.2 (57.3 - 140.7) pg/ml, and for TLH group (range) was 230.9 (114.8 - 445.3) pg/ml, 147.7 (66.4 - 223.4) pg/ml and 131.2 (81.7 - 193.7) pg/ml preoperative, 1 hour postoperative, and 24 hours post-operation respectively ($P < 0.05$, Fig. 1). The median CRP level for TAH group (range) was 8.5 (6.65 - 12.2) mg/l, 8.5 (6.75 - 12.95) mg/l and 8.5 (7.85 - 10.05) mg/l, and for TLH group (range) was 9.6 (8.5 - 11.1) mg/l, 9.4 (6.7 - 13.1) mg/l and 10.1 (7.3 - 28.1) mg/l preoperative, 1 hour postoperative, and 24 hours post-operation respectively ($P < 0.05$, Fig. 2). Median Cortisol level for TAH group (range) was 22.1 (18.33 - 35.085) µg/dl, 19.6 (18.1 - 30.2) µg/dl and 19.5 (16.6 - 37.5) µg/dl, and for TLH group (range) was 20.3 (19.1 - 30.5) µg/dl, 18.9 (16.1 - 27.4) µg/dl and 17.6 (16.6 - 23.2) µg/dl preoperative, 1 hour postoperative, and 24 hours post-operation respectively ($P < 0.05$, Fig. 3).

3.2. Discussion

Trauma that is caused by surgery, especially a large operation, sets off a chain reaction of hormonal, metabolic, and inflammatory changes that come together to produce the stress response. The stimulation of the afferent neural and sympathetic nerve systems, in addition to the presence of physiologically strong inflammatory mediators such as cytokines, are the factors that contribute to the development of this surgical stress response. Among all the pro inflammatory cytokines, interleukin-6 (IL-6) is the principal mediator that is created shortly after surgical injury. It plays an important and early role in both the local and systemic inflammatory response. Multiple studies, most notably the one that was carried out by Cruickshank et al. in 1990, have shown that the levels of IL-6 are directly connected with the degree of direct surgical tissue injury as well as the duration

of the operation. The amount of this mediator that is able to reach systemic circulation is directly proportional to degree of damage that has been done to the tissues. As a result, it has the potential to act as a useful signal regarding the evaluation of different surgical procedures that are used for the same purpose [11]. When it comes to the mean levels of IL-6 in both study groups, test of between-subjects effects indicates that there is a statistically significant difference between groups (F = 5.477, df = 1, P value = 0.029). According to findings of within-subjects effects test, there is a statistically significant influence of time (F = 7.295, df = 4, P value = 0.003), but there is no statistically significant interaction between group and time (F = 1.218, df = 4, P value = 0.302).

A test of between-subjects effects reveals that there is no statistically significant difference between the two study groups in terms of the median levels of IL-6. The P value for this test is 0.079, which shows that there is no difference between the groups. There was a statistically significant influence of time (P value = 0.001), according to the findings of the within-subjects effects test; however, there was no statistically significant interaction between the group and the time (P value = 0.813). A statistically significant difference was not identified between the two groups in terms of the area under the curve (AUC), time-weighted average (TWA), minimum and maximum levels of interleukin-6 (IL-6), as determined by serial measurement analysis (P < 0.05) [12]. According to the results of the test of between-subjects effects, there is not a statistically significant difference between the two study groups in terms of the mean CRP levels (F = 1.137, df = 1, P value = 0.298). This is the conclusion that can be drawn from the data analysis. According to the findings of the analysis of within-subjects effects, there is no statistically significant influence of time (F = 1.423, df = 4, P value = 0.250), and there is also statistically insignificant interaction between group and time (F = 1.266, df = 4, P value = 0.293). As far as the median CRP in both research groups is concerned, the results of the test of between-subjects effects reveal that there is statistically insignificant difference between groups (P value = 0.179). A statistically significant influence of time not found (P value = 0.156), and there was also statistically insignificant interaction between group and time (P value = 0.930). This was determined by an evaluation of impacts that occurred within individuals themselves. As a result of this inquiry, serial measurement analysis for CRP revealed that there was no statistically significant difference between two groups in terms of area under curve (AUC), time weight attained (TWA), and lowest and maximum values of CRP (P < 0.05). In terms of mean cortisol levels in both study groups, test of between-subjects effects reveals that there is statistically insignificant difference between groups (F = 0.788, df = 1, P value = 0.384). This is conclusion that can be drawn from the data. According to findings of the analysis of within-subjects effects, there is no statistically significant influence of time (F = 0.675, df = 4, P value = 0.517), and there is also statistically insignificant interaction between group and time (F = 0.410, df = 4, P value = 0.671). In terms of median cortisol levels in both of the study groups, the results of test of between-subjects effects suggest that there is statistically insignificant difference between groups (P value = 0.675). A statistically significant influence of time not found (P value = 0.348), and there was also statistically insignificant interaction between group and time (P value = 0.543). The results of serial measurement analysis carried out in this study revealed that there was statistically insignificant difference between two groups in terms of the area under curve (AUC), time weighted average (TWA), minimum and maximum cortisol levels (P < 0.05). These results may be attributed to highly skilled surgeons performing total abdominal hysterectomy (TAH) in this research, significantly longer surgical duration in total laparoscopic hysterectomy (TLH) compared to TAH, and fact TLH is a relatively novel technique performed in a teaching hospital. These variables may have influenced levels of neuroendocrine and inflammatory markers in study. Mean anesthesia time for TAH group (± SD) was 198.33 ± 43.13 minutes, IQR (172.5 - 230.0 min), mean anesthesia time for TLH group (± SD) was 196.67 ± 64.54 minutes, IQR (130.0 - 250.0 min); Mean operative time for TAH group (± SD) 154.58 ± 42.18 minutes, IQR (135.0 - 182.5 min), mean operative time for TLH group (± SD) 155.83 ± 62.99 minutes, IQR (95.0 - 210.0 min). Hospital stay was shorter in TLH group than TAH group, but this difference not statistically significant. Major or minor complications in both groups were non-significant. In [13] which is a randomized controlled study comparing clinical outcome and tissue trauma after laparoscopic and abdominal hysterectomy, where fifty women scheduled for hysterectomy randomized to undergo either laparoscopic (n=25) or abdominal (n=25) hysterectomy. Surgical characteristics, hospital stay, convalescence and complications were analyzed. Blood samples for assay of markers of tissue trauma (interleukin-6, C-reactive protein, tumor-associated trypsin inhibitor and tumor-associated antigen CA 125) were taken preoperatively, on the first, second and seventh postoperative day and at the follow-up visit four weeks after surgery. In the LH group, there was one conversion to abdominal hysterectomy because of severe pelvic adhesions. Five women had postoperative pelvic infection and two of them were re hospitalized for four and seven days. In the AH group, two reoperations on the day of surgery were performed: one laparotomy because of bleeding from the uterine artery and one vaginal suturing to stop vaginal cuff bleeding. One woman developed infection of the vaginal vault and four women had wound infection; two of them were hospitalized for two and five days. So, for tissue trauma analysis 18 uncomplicated hysterectomies in both groups were included. Six women with the above-mentioned complications were excluded from the LH group and in addition one woman with an elevated preoperative CA 125 level (216 kU/L) for no apparent reason [14]. Compared with preoperative values, IL-6 levels were increased significantly in both groups on first postoperative day. Concentration had decreased to preoperative value by second postoperative day in the LH group and by seventh postoperative day in the AH group. Level of IL-6 was significantly higher in the AH group on first and on second postoperative day compared with LH. Concentrations of CRP were also elevated from preoperative values and increase was highest on second postoperative day in both groups. Mean IL-6 level for AH group (± SD) was 4.4 ± 2.8 pg/ml, 21.6 ± 15.1 pg/ml, 17.0 ± 18.4 pg/ml, 4.8 ± 3.6 pg/ml, 3.7 ± 0 pg/ml, and for LH group (± SD) was 3.7 ± 0 pg/ml, 10.4 ± 8.8 pg/ml, 5.5 ± 3.9 pg/ml, 4.4 ± 2.2 pg/ml, 3.7 ± 0 pg/ml, preoperatively, on first, second, seventh and after 28th days postoperative respectively. Mean CRP level for AH group (± SD) 0.7 ± 0.9 mg/l, 21.8 ± 12.0 mg/l, 55.3 ± 26.0 mg/l, 15.0 ± 15.9 mg/l, 1.4 ± 1.3 mg/l, and for LH group (±

SD) was 1.4 ± 1.9 mg/l, 12.1 ± 14.1 mg/l, 26.5 ± 21.3 mg/l, 10.4 ± 13.2 mg/l, 1.8 ± 2.3 mg/l, preoperatively, on first, second, seventh and after 28th days postoperative respectively. Mean operating time and anesthetic time were significantly longer in laparoscopic group, and time of hospital stay was significantly shorter in association with laparoscopic hysterectomy. There were no significant differences in postoperative complications between study groups and no major complications occurred ($p < 0.05$). Mean anesthesia time for TAH group (± SD) 82.7 ± 14.7 min, and for TLH group (± SD) was 122.1 ± 16.1 min. Mean operative time for TAH group (± SD) was 57.5 ± 12.5 min, and for TLH group (± SD) was 85.3 ± 13.5 min. Mean hospital stay for TAH group (± SD) was 3.4 ± 0.7 days, and for TLH group (± SD) was 2.1 ± 0.3 days (13). Ribeiro et al. [15] performed a randomized study of total abdominal, vaginal and laparoscopic hysterectomy, where sixty patients referred for hysterectomy prospectively randomized to total abdominal hysterectomy (n=20), vaginal hysterectomy (n=20), or laparoscopic hysterectomy (n=20). The operative time, blood loss (variation in erythrocyte and hemoglobin) and inflammatory answer (CRP and interleukin-6 dosages) were compared by using Kruskal–Wallis, Dunn non-parametric test and variance analysis with repeated measurements. CRP levels increased steadily from vaginal hysterectomy to laparoscopic hysterectomy and then to total abdominal hysterectomy. Increase in interleukin-6 was substantially higher in total abdominal hysterectomy, whereas no differences noted between vaginal and laparoscopic hysterectomy. Mean IL-6 for AH group (± SD) was -2.85 ± 9.00 pg/ml, 42.84 ± 34.48 pg/ml, 59.75 ± 117.05 pg/ml, 18.63 ± 19.86 pg/ml, 3.87 ± 11.16 pg/ml, and for LH group (± SD) was -4.95 ± 6.31 pg/ml, 26.97 ± 17.77 pg/ml, 31.03 ± 31.94 pg/ml, 15.16 ± 20.71 pg/ml, -1.05 ± 6.63 pg/ml, preoperatively at beginning of anesthesia, immediately after end of surgery, 24 and 48 h after surgery, and on sixth day after surgery respectively. Mean CRP for AH group (±SD) was 3.21 ± 3.56 mg/dl, 14.42 ± 42.84 mg/dl, 67.46 ± 43.62 mg/dl, 97.05 ±34.37 mg/dl, 34.71 ± 32.34 mg/dl, and for LH group (±SD) was 3.43 ± 1.80 mg/dl, 4.62 ± 6.63 mg/dl, 67.93 ±67.03 mg/dl, 61.87 ± 45.80 mg/dl, 15.84 ± 14.96 mg/dl, preoperatively at beginning of anesthesia, immediately after end of surgery, 24 and 48 h after surgery, and on sixth day after surgery respectively. The average operative time in TAH, VH and LH was 109 min, 78 min, and 119 min, respectively. VH operative time was significantly shorter than TAH and LH (P = 0.001) and there was no significant difference between LH and TAH. In one patient of VH group with history of three cesareans, operative time was prolonged due to difficulty in dissecting vesicouterine space and need of repairing a 2 cm bladder injury [15]. Demir et al. [16] is a prospective randomized study that was undertaken at the Dokuz Eylül University Hospital, Department of Obstetrics and Gynecology, where patients were randomized in accordance with a computer-generated sequence and TLH, LH and AH performed on 15 patients each for benign reasons. Blood samples of 6 ml were collected from veins of patients preoperatively, at the immediate postoperative time and postoperative 24th hour. There was no significant difference in the preoperative and immediate postoperative serum levels of CRP and IL-6 concentrations among all groups. However, 24th hour levels of CRP and IL-6 were significantly higher in the AH group than in each of the laparoscopy groups (P = 0.00 and P = 0.00 for CRP and IL-6, respectively). The median IL-6 level for AH group (range) was 2.00 (2.00 - 4.75) pg/ml, 6.62 (2.00 - 33.43) pg/ml and 47.16 (31.34 - 174.10) pg/ml, and for TLH group (range) was 2.00 (2.00 - 5.25) pg/ml, 9.13 (2.79 - 65.93) pg/ml and 31.64 (8.85 - 87.00) pg/ml preoperative, immediately postoperative, and 24 hours post-operation respectively. The median CRP level for AH group (range) was 1.65 (0.45 - 4.98) mg/l, 1.71 (0.45 - 6.97) mg/l and 91.57 (34.41 - 145.97) mg/l, and for TLH group (range) was 1.11 (0.12 - 4.33) mg/l, 1.28 (0.21 - 4.16) mg/l and 38.40 (13.82 - 95.71) mg/l preoperative, immediately postoperative, and 24 hours post-operation respectively. There was a statistically significant difference between AH and TLH as regard operative time "which significantly longer in TLH group", and duration of hospital stay "which was significantly shorter in TLH group" ($p < 0.05$). The median operative time for AH group (range) was 94 (44 - 127) min, and for TLH group (range) was 103 (67 - 245) min. Median duration of hospital stay for AH group (range) was 94 2 (1 - 6) days, and for TLH group (range) was 1 (0 - 4) days (16). Kim & Yoon [11] a clinical, single Centre study comparing neuroendocrine and inflammatory responses after laparoscopic and abdominal hysterectomy. Where twenty-four patients with no major medical disease were randomly assigned to undergo laparoscopic (n = 13) or abdominal hysterectomy (n = 11). Venous blood samples collected from each patient at following times: a baseline sample before surgery (T0), after skin incision (T1), at end of peritoneum closure (T2), 1 h after operation (T3) and 24 h after operation (T4). Statistical analysis was performed using Sigma stat (version 2.03, SPSS, Chicago, IL). Before operation, the serum IL-6 level was not detected in both groups. However, the levels of IL-6 rose significantly after surgery in both groups. As the surgery proceeded, the changes of IL-6 showed a similar pattern between the groups: level increased at end of peritoneum closure and it reached peak value at 1 hr. postoperatively. For patients who underwent abdominal hysterectomy, the peak IL-6 concentration was significant higher than peak IL-6 levels of patients who underwent laparoscopic hysterectomy (P < 0.05). The IL-6 level in abdominal hysterectomy group remained significantly elevated for 24 hr. postoperatively, and this was longer than that in laparoscopic hysterectomy group (P < 0.05). Serum concentration of CRP did not increase throughout operation or at 1hr postoperatively, but there was an abrupt significantly higher increase at 24 hr. after operation in both groups. CRP concentration at 24 hr. postoperatively was 10.8 mg/l in patients who underwent laparoscopic hysterectomy as compared to that of patients who underwent abdominal hysterectomy (39.5 mg/l) (P < 0.05) and correlation with between cytokine and CRP. For serum cortisol level, baseline serum cortisol level was no difference between groups and groups had similar sequential changes over time throughout operation and 24 hr. after operation. The serum cortisol level increased after surgery started, it reached its peak level at 1 hr. postoperatively in patients undergoing abdominal hysterectomy, but it reached its peak level at end of peritoneum closure in patients who undergoing laparoscopic hysterectomy. Although the serum cortisol level did not show a significant difference between groups, more rapid decline to baseline (from 30.4 ± 7.7 μg/dl to 11.8 ± 3.6 μg/dl) after operation and (from 38.0 ± 14.3 μg/dl to 18.1 ± 5.9 μg/dl) in patients who underwent abdominal hysterectomy.

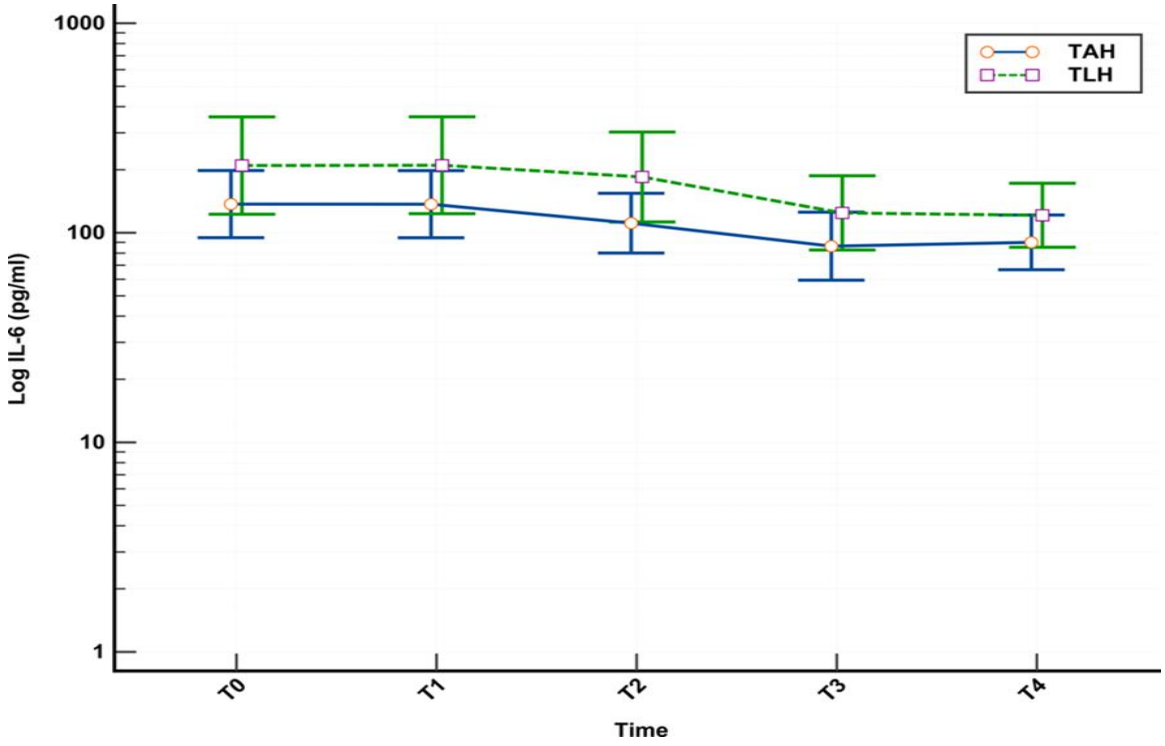

Fig. (1): Change in Il-6 level in both study groups. Data are log-transformed because assumption of normality was not met. Error bars represent 95% confidence interval (95% CI). Test of between-subjects is not statistically significant (p-value = 0.079). Test of within-subjects effects shows a statistically significant effect of time (p- value = 0.001) with no statistically significant group * time interaction (p- value = 0.813).

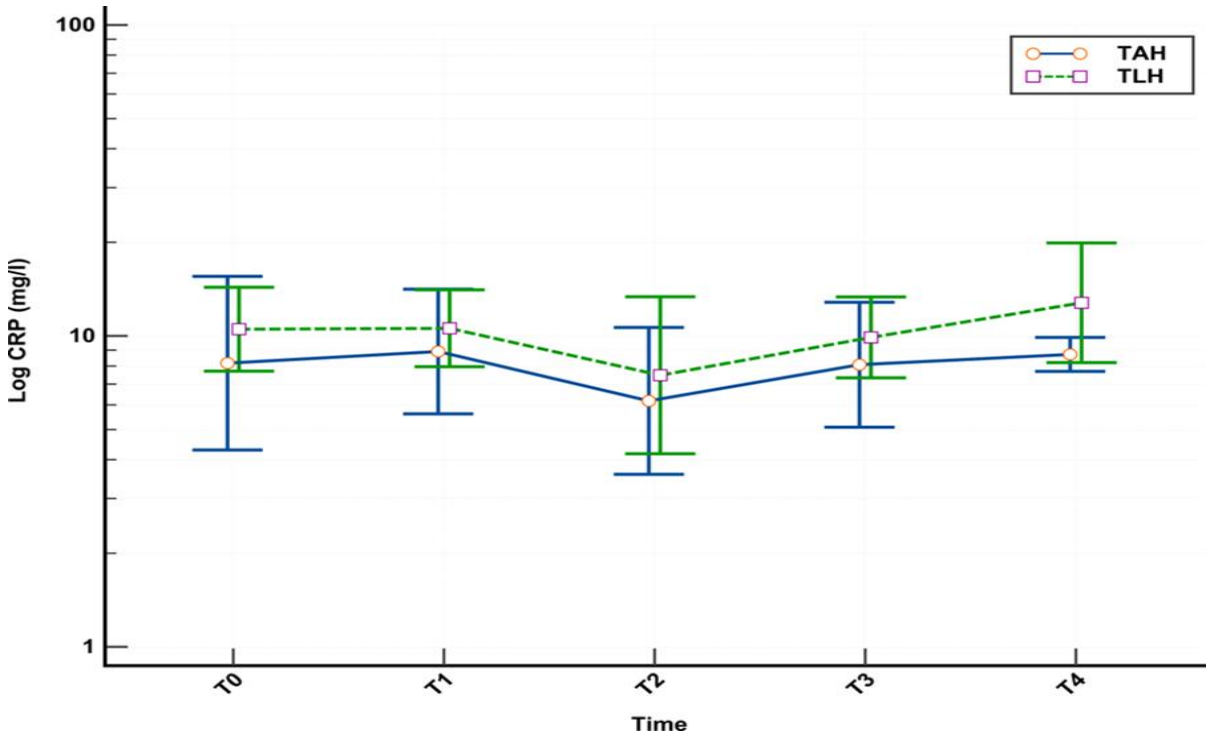

Fig. (2): Change in CRP level in both study groups. Data are log-transformed because assumption of normality was not met. Error bars represent 95% confidence interval (95% CI). Test of between-subjects is not statistically significant (p-value = 0.179). Test of within-subjects effects shows no statistically significant effect of time (p- value = 0.156) with no statistically significant group * time interaction (p- value = 0.930).

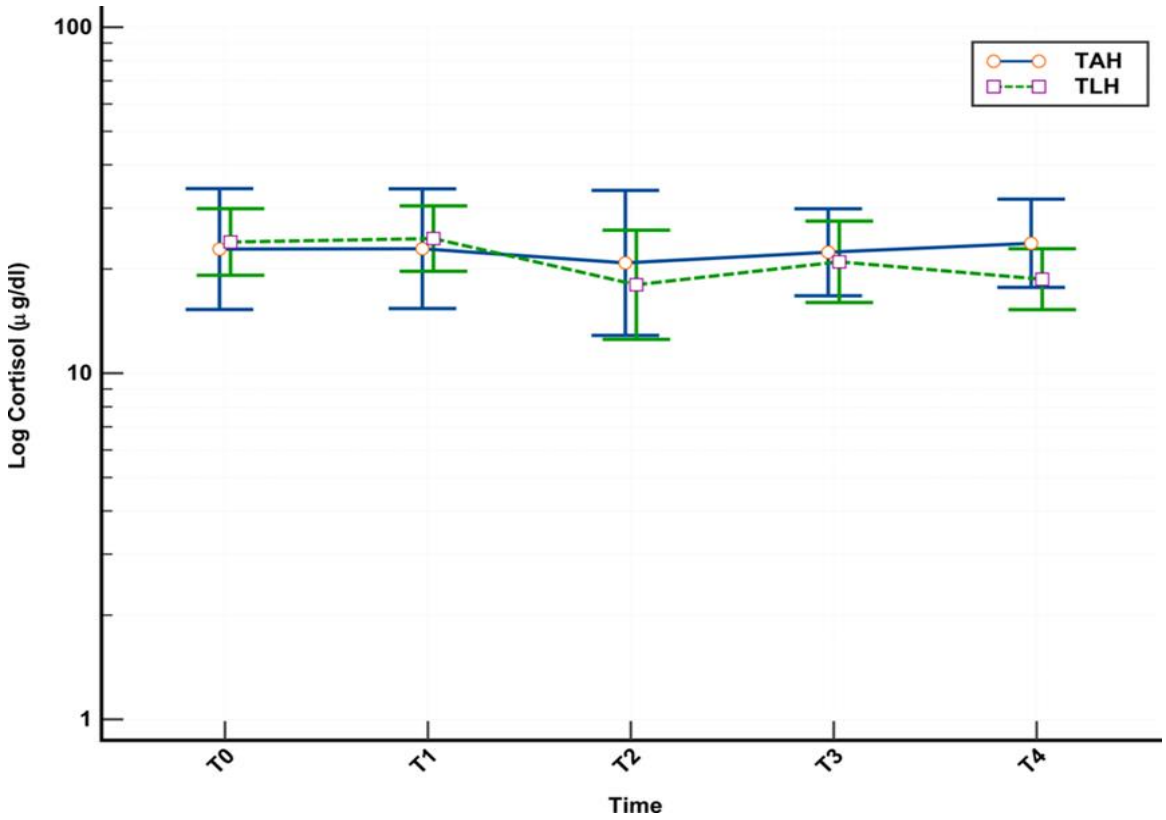

Fig. (3): Change in Cortisol level in both study groups. Data are log-transformed because assumption of normality was not met. Error bars represent 95% confidence interval (95% CI). Test of between-subjects is not statistically significant (p-value = 0.675). Test of within-subjects effects shows no statistically significant effect of time (p- value = 0.348) with no statistically significant group * time interaction (p- value = 0.543).

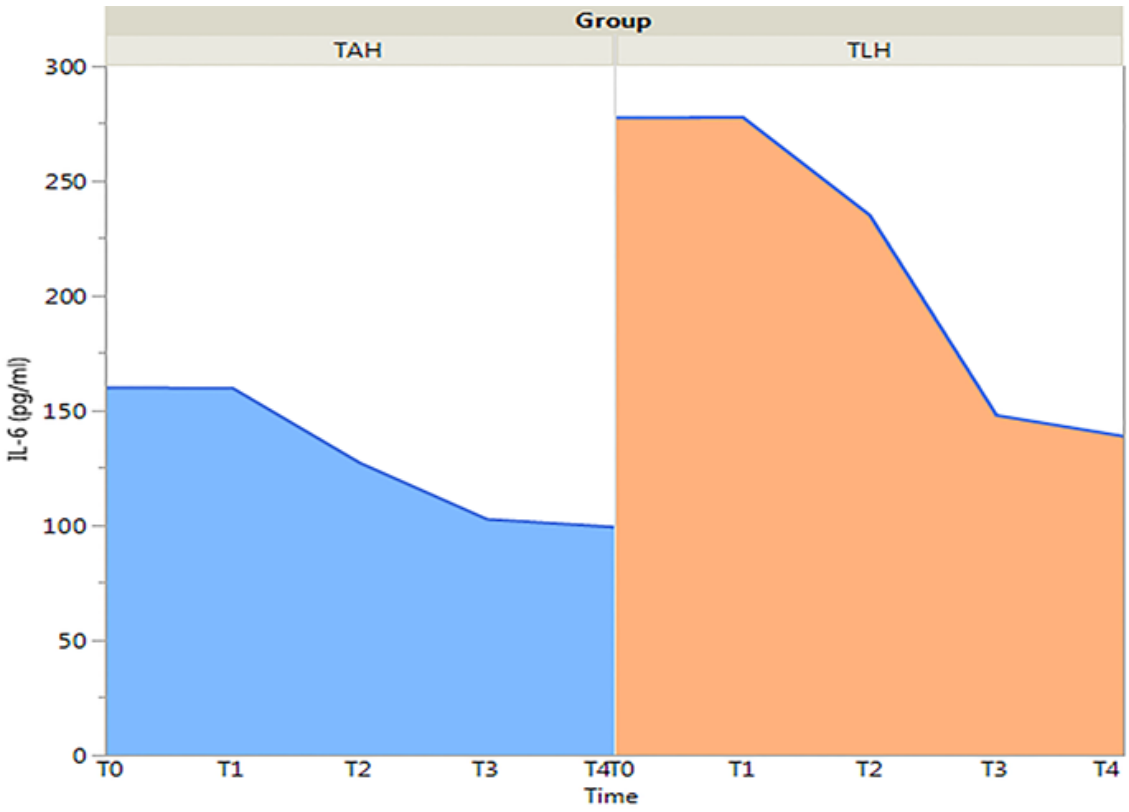

Fig. (4): Serial measurement diagram plot showing the area under the time-IL-6 curve. Minimum value, maximum value, time-weighted average (TWA), and area under the curve (AUC) are all comparable in both groups (p-value = 0.089, 0.068, 0.060 and 0.060, respectively).

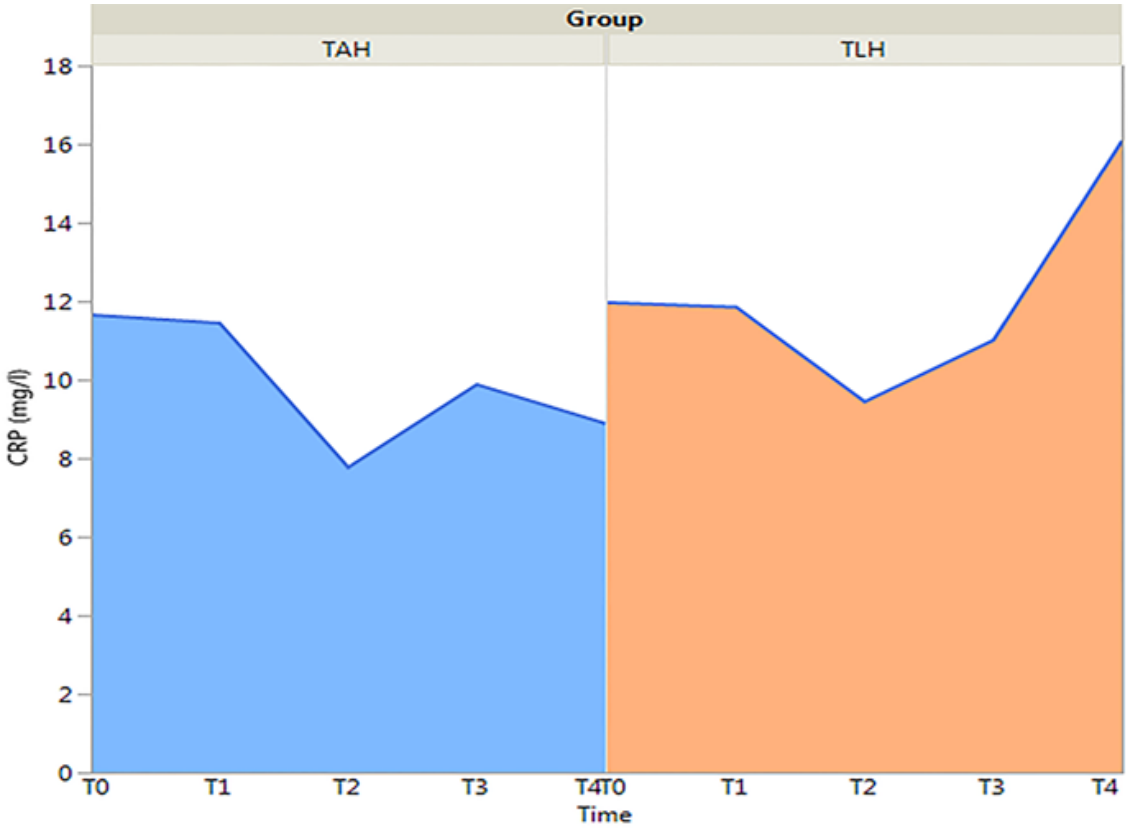

Fig. (5): Serial measurement diagram plot showing the area under the time-CRP curve. Minimum value, maximum value, time-weighted average (TWA), and area under the curve (AUC) are all comparable in both groups (p-value = 0.149, 0.204, 0.178 and 0.178, respectively).

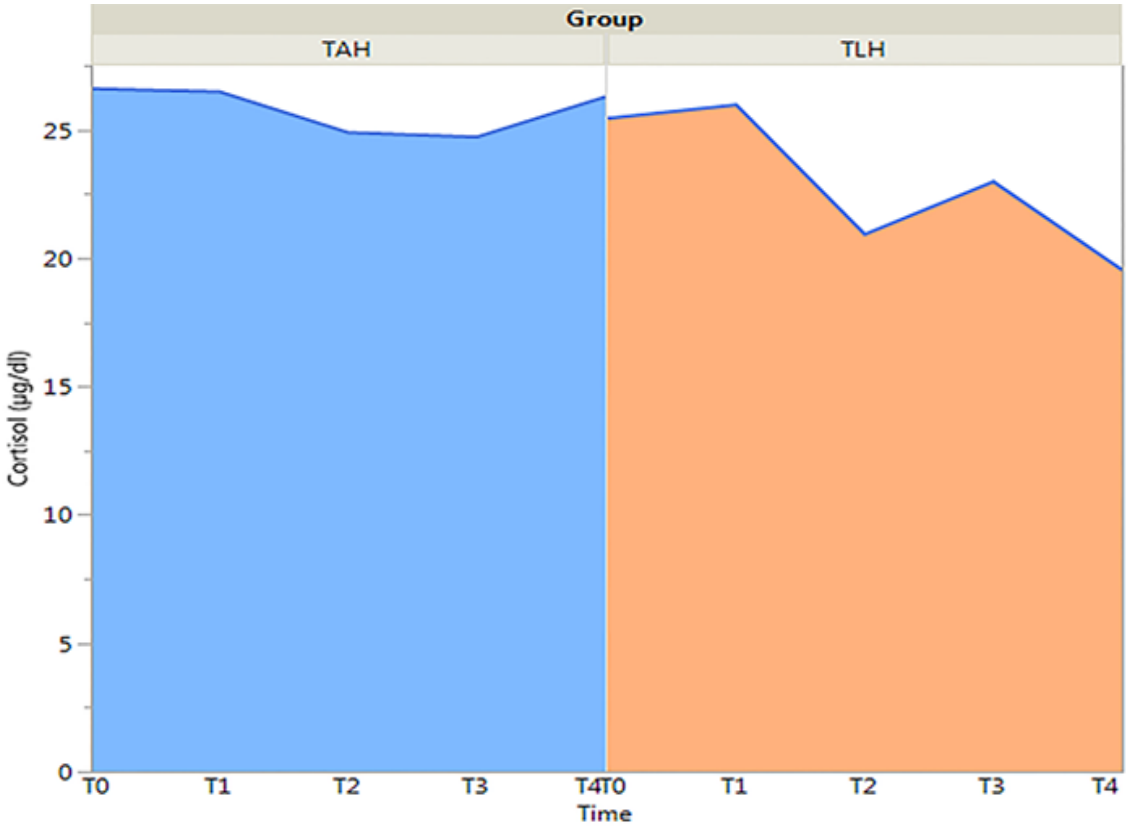

Fig. (6): Serial measurement diagram plot showing the area under the time-Cortisol curve. Minimum value, maximum value, time-weighted average (TWA), and area under the curve (AUC) are all comparable in both groups (p-value = .242, .478, .378 and .378, respectively).

Table (1): Demographic characteristics of both study groups

	TAH (N=12)	TLH (N=12)	t-test	P-value†
Age (years, mean ± SD	44.5 ± 4.96	47.58 ± 6.33	1.328	0.198
BMI (kg/m^2, mean ± SD	30.25 ± 4.45	31.67 ± 3.8	0.838	0.411

Table (2): Operative data in both study groups

	TAH (N=12)	TLH (N=12)	t-test	P-value†
Anesthesia duration (min, mean ± SD)	198.33 ± 43.13	196.67 ± 64.54	0.074	0.941
Surgery duration (min, mean ± SD)	154.58 ± 42.18	155.83 ± 62.99	0.057	0.955
Hospital stay (days, mean ± SD)	3.92 ± 2.5	3.33 ± 1.23	0.724	0.476

But there was no significant difference for this between groups. There was correlation with between cytokine and CRP levels (Pearson correlation coefficient r = 0.796; P < 0.05). No significant difference between two groups was shown with respect to operation time and duration of anesthesia. Mean anesthesia time for TAH group (± SEM) was 151.8 ± 14.1 min, and for TLH group (± SEM) was 188.61 ± 37.9 min. Mean operative time for TAH group (± SEM) was 122.7 ± 11.2 min, and for TLH group (± SEM) was 141.4 ± 41.5 min. But for hospital stay, there was a statistically significant difference between two groups as regard duration of hospital stay, which was significantly shorter in the TLH group. The mean duration of hospital stay for TAH group (± SEM) was 7.9 ± 0.2 days, and for TLH group (± SEM) was 5.6 ± 0.5 min [11]. Oksuzoglu et al. [17] performed a prospective clinical study comparing tissue trauma after abdominal, vaginal and total laparoscopic hysterectomy; seventy-one patients requiring hysterectomy for benign uterine diseases enrolled in the study and divided into three treatment groups: AH (n=24), VH (n=23), and TLH (n=24). Blood samples for assay of interleukin-6 (IL-6) and creatine phosphokinase (CPK) collected pre-, intra-operatively, and 2, 6 and 24 h after surgery. Serum levels of IL-6, and CPK significantly elevated over basal values after surgery in all groups. IL-6 levels significantly higher after AH as compared to VH and TLH. IL-6 concentrations were significantly higher in VH group than TLH group (p=0.001).

The values of IL-6 (pg/ml) given as median and (range) for AH was 2.1 (2-60.3), 6.6 (2-141), 22.7 (2-109), 39.2 (2-120), 35 (2-100), for VH was 2 (2-16.2), 2.7 (2-28.2), 19.7 (2-74.2), 34.1 (5.6-247), 21.6 (5.4-78), and for TLH was 4.1 (2-20), 7.8 (2-21.4), 12.8 (2-23.8), 11.5 (3.5-27), 15 (6.2-58) preoperatively, intra operatively (on peritoneal closure), and 2, 6 and 24 h after surgery respectively. Longer anesthesia and operation time reported in TLH group than both AH and VH groups, but average hospital stay for TLH group was shorter than other two groups ($p < 0.01$). Mean anesthesia time for TAH group (± SD) was 100 ± 17.8 min, for VH group was 109.7 ± 18.6 min, and for TLH group (± SD) was 137.5 ± 33.4 min. Mean operative time for TAH group (± SD) was 90.3 ± 16.7 min, for VH group was 101.3 ± 17.2 min, and for TLH group (± SD) was 128.1 ± 32.6 min. Mean hospital stay for TAH group (± SD) was 3.2 ± 0.5 days, for VH group was 3.2 ± 0.5 days, and for TLH group (± SD) was 2.5 ± 0.5 days [17]. Oranratanaphan et al. [18] performed a comparative study of quality of life of patients who underwent TLH and TAH. Total 100 cases of TAH and 102 cases of TLH collected. General characteristics and operative procedure including complications also recorded. TLH may help in short term improvement in some aspect of quality of life after surgery. Long term benefit in quality of life is not significant. However, TLH still has benefits in reduced blood loss and hospital stay compared to TAH [18].

4. Conclusions

In conclusion this study demonstrates that inflammatory response after total abdominal hysterectomy "TAH" and total laparoscopic hysterectomy "TLH" is equal as shown by measuring IL-6, CRP & Cortisol. Teaching might have impact on advantages of laparoscopic surgeries in comparison to open surgeries. Simulation training might help speed teaching curve and improve performance and consequently patients' outcomes. As laparoscopic hysterectomy appeared to be superior to abdominal hysterectomy as regard duration of hospital stay, return to normal activities, satisfaction, and quality of life. Further studies including large number of cases are needed to confirm the efficacy of TLH versus TAH under the previous aspects, but in complicated cases as those complaining of endometriosis, malignancies, many previous uterine or abdominal incisions …. Etc. Major long-term complications (i.e. fistula, pelvi-abdominal pain, urinary dysfunction, bowel dysfunction, pelvic floor condition and sexual dysfunction) in both types of operations need to be assessed and monitored. Also several further studies are needed to confirm the efficacy of robotic hysterectomy.

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