

**EFFECTIVENESS OF ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS
PLANE BLOCK IN PELVIC GYNAECOLOGICAL SURGERY AT KENYATTA
NATIONAL HOSPITAL**

DISSERTATION SUBMITTED IN PART FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF MASTER OF MEDICINE IN ANAESTHESIA OF THE
UNIVERSITY OF NAIROBI

PRINCIPAL INVESTIGATOR:

DR. FAITH KERUBO OGARI MBChB (UoN)

DECLARATION

I hereby declare that this dissertation is my original work and that it has not been submitted to any university or institution for examination or any other purposes.

Signed _____ Date _____

Ogari Faith Kerubo (UoN)

Post-graduate student in Anaesthesia

University of Nairobi registration number: H58/69749/2013

Supervisors:

Dr. Thomas Chokwe

MBChB, MMed Anaesthesia (UoN)

Lecturer in Anaesthesiology; Department of Anaesthesia, UoN.

Signed _____ Date _____

Dr. Timothy Mwiti

MBChB(MOI), MMed Anaesthesia (UoN)

Lecturer in Anaesthesiology; Department of Anaesthesia, UoN.

Signed _____ Date _____

Dr. Anthony Gatheru

MBChB, MMed Anaesthesia (UoN)

Lecturer in Anaesthesiology; Department of Anaesthesia, UoN.

Signed _____ Date _____

Dr. Thomas Chokwe

MBChB, MMed Anaesthesia (UoN)

Chairman department of Anaesthesia, UoN.

Signed _____ Date _____

DEDICATION

To my parents Chrisantus Ogari and Rael Ogari for their love, prayers and sacrifice to educate and prepare me for the future. They are the ultimate role models.

My husband Caleb Ndege for his unreserved love, support and inspiration and our wonderful children Jewel and Jaison for enduring the long days and nights that I was away for study.

ACKNOWLEDGEMENT

I wish to express my sincere gratitude to:

The Almighty God, for the gift of life, good health, strength and perseverance

My supervisors, Dr. T. Chokwe, Dr. T. Mwititi and A. Gatheru for their unreserved support, invaluable constructive criticism and guidance from the drafting of the proposal to the final dissertation

Colleagues in the department of Anaesthesia and friends for their constant encouragement and input.

To the staff members of ward 1B and gynaecology theatre for their support

TABLE OF CONTENT

DECLARATION	ii
TABLE OF CONTENT	vi
LIST OF FIGURES	viii
LIST OF TABLE	ix
LIST OF ABBREVIATIONS	x
ABSTRACT.....	xi
CHAPTER ONE: INTRODUCTION	1
1.1 Background Information	1
1.2 Research Questions	3
1.3 Research Objectives	4
1.4 Justification	4
CHAPTER TWO: LITERATURE REVIEW	6
2.1 Physiology of pain.....	6
2.2 History of TAP block	7
2.3 Anatomy	8
2.4 Indications of TAP block	9
2.5 Contraindications	10
2.6 Monitoring the analgesic effectiveness	11
2.7 Efficacy of TAP block.....	12
CHAPTER THREE: RESEARCH METHODOLOGY	16
3.1 Research Design	16
3.2 Study Area and Target Population	16
3.3 Exclusion and inclusion criteria	16
3.4 Sample Size Determination and Sampling Procedure.....	17
3.5 Study procedure.....	17
3.6 Operational Definitions	19
3.7 Data Collection Procedure	20
3.8 Data Analysis	20
3.9 Ethical Considerations.....	21
CHAPTER FOUR: STUDY RESULTS	22
4.1 Demographic characteristics	22
4.2 BMI	23

4.3	Type of pelvic gynaecological surgery	24
4.4	Indication for the surgery	25
4.5	Induction drugs.....	25
4.6	Maintenance/ Analgesia	26
4.7	Blood pressure.....	27
4.8	Heart Rate.....	27
4.9	Post-operative pain management	28
4.10	Anaesthesia providers	28
4.11	Pain scores.....	28
4.12	Time to request analgesia.....	29
4.13	Time to ambulation	30
4.14	Complications.....	31
4.15	Relationship between Pain scores and maintenance combination analgesia	31
4.16	Relationship between Pain scores and post-operative management	31
CHAPTER FIVE: DISCUSSION.....		32
5.1	Discussion	32
5.3	Recommendations	36
5.4	Limitations	36
APPENDICES		37
REFERENCES		37

LIST OF FIGURES

Figure 1: Schematic view of an ultrasound guided transversus abdominis block	3
Figure 2: Anatomy of the abdominal wall	8
Figure 3: Image of the abdominal wall	9
Figure 4: Correct local anaesthetic deposition in the transversus abdominis plane	20
Figure 5: Distribution of age in years	22
Figure 6: BMI Distribution	24
Figure 7: Requested vs unrequested (a)	29
Figure 8: Requested vs unrequested (b)	30
Figure 9: Requested vs unrequested (c)	30

LIST OF TABLES

Table 1: Demographic characteristics.....	23
Table 2: BMI.....	23
Table 3: Type of pelvic gynaecological surgery	25
Table 4: Indication for the surgery.....	25
Table 5: Induction drugs	26
Table 6: Maintenance/ Analgesia drugs.....	26
Table 7: Blood pressure percentage changes	27
Table 8: Heart Rate change in percentage	27
Table 9: Post-operative pain analgesia combination.....	28
Table 10: Anaesthesia providers	28
Table 11: Pain scores	29
Table 12: Time to request analgesia	29

LIST OF ABBREVIATIONS

ASA:	American Society of Anaesthesiologists
BMI:	Body Mass Index
DVT:	Deep Vein Thrombosis
KNH:	Kenyatta National Hospital
LAI:	Local Anaesthetic Infiltration
NIPC:	National Initiative on Pain Control
PONV:	Postoperative Nausea and Vomiting
RCT:	Randomized Control Trials
SPSS:	Statistical Package for the Social Sciences
TAP:	Transverse Abdominis Plane
VAS:	Visual Analogue Scale
IV	Intravenous
IM	Intramuscular
PR	Per Rectum
PRN	pro re nata (as needed)

ABSTRACT

Background: Goals of postoperative pain management are to relieve suffering, achieve early mobilization, prevent postoperative complications, reduce length of hospital stay, achieve patient satisfaction and prevent chronic pain syndromes. Regional anaesthesia reduces the risk of chronic pain post-surgery compared to conventional pain control. A multimodal approach to adequate post-operative analgesia includes regional blocks of the anterior abdominal wall and local infiltration of the incision site. There is an increased risk of DVT in pelvic surgery and therefore the need to ambulate as soon as possible. Inadequate post-op pain management especially during the first 24hrs has been associated with development of chronic pain syndromes.

Objectives: To assess post-operative pain relief following pelvic gynaecological surgeries using TAP block at KNH for the first 24 hours

Methodology: This study adopted an observational study design involving adult women undergoing elective pelvic gynaecological surgery at KNH for a period of 3 months. It assessed the pain scores of the respondents immediately after the surgery and a follow up for at 6,12,18,24 hours post operatively, time to ambulation and need for rescue analgesia. It utilized 43 adult women.

Data was collected using questionnaires administered by the researcher with the help of trained research assistants. All data collected in the study was sorted, coded and entered in a computer using SPSS version 20. Descriptive statistics such as mean, median and measures of dispersion were used to describe the VAS scores of the patients receiving TAP block while frequencies and percentages were used to describe analgesic requirements and time to ambulation. The study findings were presented using figures, tables, pie-charts and bar-graphs.

Results: The overall average pain score was 2(mild pain) and the average time to request analgesia was 9 hours post operatively .12 patients did not request for rescue analgesia therefore reducing their opioid requirements.33 patients requested for analgesia 15 were given tramadol 9 morphine and 6 paracetamol .3 were not given.The average time to complete ambulation was noted to be 18 hours. Nausea, Vomiting and Diarrhoea were the side effects experienced post operatively, though they are more likely to be attributed to the anaesthetics and analgesics given.

Conclusion: single shot bilateral ultrasound guided **TAP** block for pelvic gynaecological surgery given together with conventional analgesics is effective in reducing pain scores for 8 to 12hrs post operatively, reduce opioid requirement, reduce rest and movement pain encouraging early ambulation with minimal side effects.

Recommendations: Routine use of ultrasound guided **TAP** block together with conventional analgesics for post operative pain management with availability of the necessary equipment needed for performing the block.

Perform a Randomized Controlled Trial to compare the effectiveness of post operative pain control between the conventional analgesics and the **TAP block**.

CHAPTER ONE: INTRODUCTION

1.1 Background Information

Pain is defined by the International Association for the Study of Pain as an unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such [1].

Pain is often classified by its pathophysiology into nociceptive and neuropathic. Nociceptive pain involves the normal neural processing of noxious stimuli that occurs when free nerve endings are activated by tissue damage or inflammation. Neuropathic pain involves the abnormal processing of stimuli from the peripheral or central nervous systems and is thought to serve no useful purpose.

Effective postoperative pain management is an integral part of modern anaesthetic practice. Goals of postoperative pain management are to relieve suffering, achieve early mobilization, prevent postoperative complications, reduce length of hospital stay, achieve patient satisfaction and prevent chronic pain syndromes [2,3].

Pain results from inflammation caused by tissue trauma or direct nerve injury and release of local inflammatory mediators that can produce augmented sensitivity to stimuli in the area surrounding the injury or sensitization of peripheral pain receptors [4]

Pelvic gynaecological surgeries are often associated with severe pain requiring a well-planned analgesia regimen to ensure adequate patient-comfort, satisfaction, early mobilization, decreased length of hospital stay and prevent chronic pain syndromes. As a significant proportion of surgical pain originates from surgical wound, use of local

anaesthetic wound infiltration or nerve blocks around the incision site would help in managing post-operative pain.

Gynaecological pelvic surgeries are also associated with high risk of development of deep venous thrombosis [5]. Regional anaesthesia reduces the risk of chronic pain post-surgery compared to conventional pain control [6]

A multimodal approach to adequate post-operative analgesia includes regional blocks of the anterior abdominal wall and local infiltration of the incision site. Anterior abdominal wall nerve blocks include the ilioinguinal, iliohypogastric, rectus sheath, and transversus abdominis plane (TAP) blocks.

The transverse abdominis plane (TAP) block is a peripheral nerve block designed to anesthetize the nerves supplying the anterior abdominal wall (T6 to L1). It was first described in 2001 by Rafi as a traditional blind landmark technique using the lumbar triangle of Petit [7]

Local anaesthetic is then injected between the internal oblique and transversus abdominis muscles just deep the fascial plane between (the plane through which the sensory nerves pass.

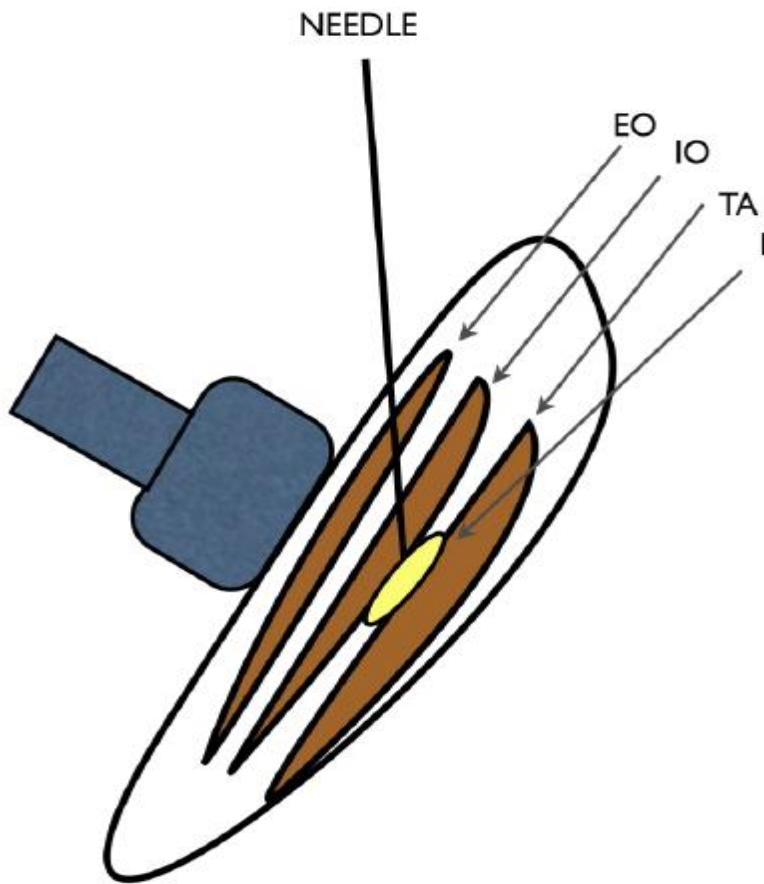


Figure 1: Schematic view of an ultrasound guided transversus abdominis block

EO – External oblique

IO – Internal oblique

TA – Transversus abdominis

LA – Local anaesthetic

1.2 Research Questions

Is post-operative pain relief with a TAP block for pelvic gynaecological surgeries at KNH adequate?

1.3 Research Objectives

Main objective

To determine the analgesic effectiveness of single-shot ultrasound guided TAP block after pelvic gynaecological surgeries at KNH in the first 24 hours.

1.3.1 Specific Objectives

- To determine the post-operative pain intensity after gynecological surgery with TAP block.
- To determine time to first request of rescue analgesia after gynecological surgery with TAP block
- To determine time to ambulation.
- To assess complication from TAP block and other pain management interventions after gynecological surgery.

1.4 Justification

Inadequate post-op pain management especially during the first 24hrs has been associated with development of chronic pain syndromes. This study therefore seeks to influence the practice of post-operative pain management in KNH to provide adequate pain management and prevent development of chronic pain syndromes. Current pain management practice at KNH is influenced by limited resources like few and overworked work force who are not able to monitor and attend to patients needs effectively.

There is an increased risk of DVT in pelvic surgery and need to ambulate as soon as possible as was shown by White RH et al in a study of incidence of symptomatic venous thromboembolism after different elective surgeries.

The results will ultimately serve to increase knowledge and more importantly quality of care provided to patients and cut on costs related to long hospital stays both to the patients and the hospital.

The study population is unique to the African population as the other studies are mainly on Caucasian population.

CHAPTER TWO: LITERATURE REVIEW

2.1 Physiology of pain

Nociception involves the 4 processes of transduction, transmission, perception, and modulation. Tissue damage releases chemical mediators, such as prostaglandins, bradykinin, serotonin, substance P, and histamine, which activate nociceptors, resulting in transduction, or the generation of an action potential. The action potential is transmitted from the site of injury along afferent nerve fibres to nociceptors at the spinal cord. Release of substance P and other neurotransmitters carry the action potential across the cleft to the dorsal horn of the spinal cord, from where it ascends the spinothalamic and spinoreticular tract to the thalamus and the midbrain. Finally, from the thalamus, fibres send the nociceptive message to the somatosensory cortex, parietal lobe, frontal lobe, and the limbic system where perception occurs which is the conscious experience of pain involving both sensory and affective component.

Modulation results from activation of the midbrain. Multiple types of neurons from this area that have a variety of neurotransmitters, including endorphins, enkephalin, serotonin (5-HT), and dimorphic, descend to lower areas in the central nervous system; these neurons stimulate the release of additional neurotransmitters, which ultimately trigger the release of endogenous opioids and inhibit transmission of the pain impulse at the dorsal horn [8]

2.2 History of TAP block

Transversus abdominis plane (TAP) block was first described by Rafi [9] and works by blocking the thoraco-lumbar nerves (T6–L1) which supply sensory fibers to the anterior abdominal wall. Although they only provide analgesia of the abdominal wall, and not the abdominal viscera, they decrease opioid requirements and post-operative nausea and vomiting.

Landmark-based 'double-pop' technique via the lumbar triangle of Petit, which accesses the nerves as they course through the fascial plane between the internal oblique and transversus abdominis muscles, was described, and has been shown to be an effective analgesic adjunct for lower abdominal surgery [10]. Blind technique however associated with high failure rates and risk of visceral injury.

Ultrasound guided TAP block first described in 2001 is increasingly being used and several modified approaches include a subcostal approach and an anterior approach at the mid-point of the 12th rib and iliac crest in the mid-axillary line.

Any landmark-based regional anesthetic technique raises issues of accuracy of placement of the needle and damage to adjacent structures. Local anaesthetic in a 'blind' technique but no published study has looked at the accuracy of injection of local anaesthetic. In TAP blocks, a landmark-based approach to the ilioinguinal/iliohypogastric nerve block was shown to result in inaccurate injection of local anaesthetic in 86% of cases in a paediatric population and also liver puncture in a patient post-Caesarean section and several case reports of colonic puncture in the paediatric population after ilioinguinal nerve block [12]

2.3 Anatomy

Innervation of the anterolateral abdominal wall arises from the anterior rami of spinal nerves T6-L1. Aim of TAP block is to deposit local anaesthetic in the plane between the internal oblique and transversus abdominis muscle targeting the spinal nerves in this plane.

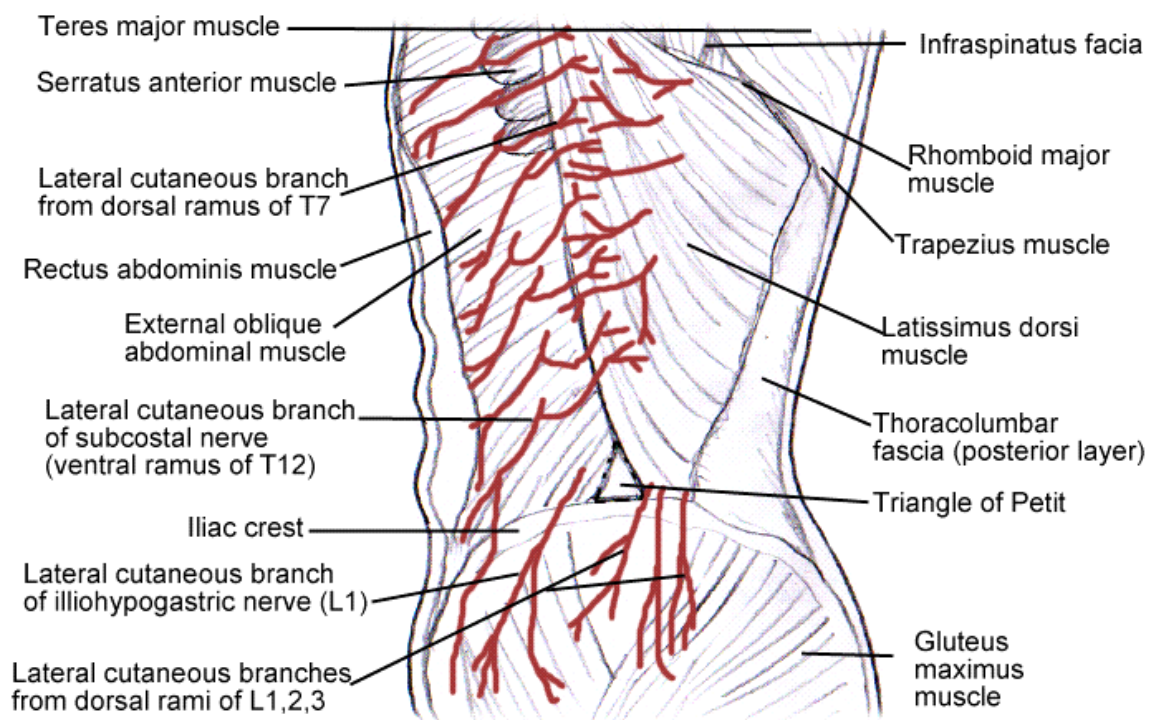


Figure 2: Anatomy of the abdominal wall

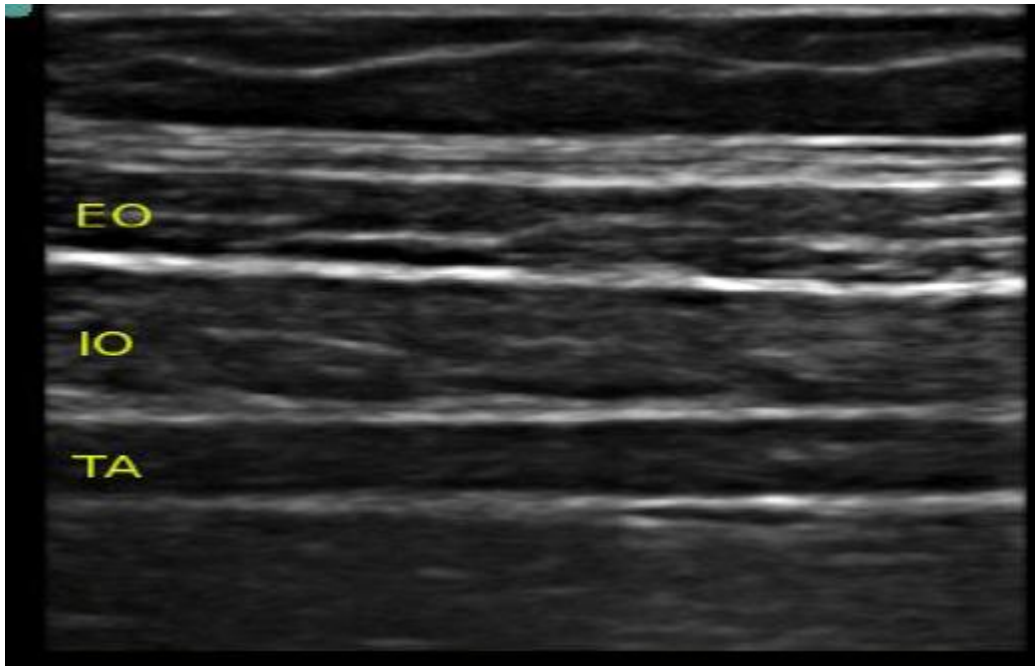


Figure 3: Image of the abdominal wall

COPYRIGHT © 2006 BY THE NEW YORK SCHOOL OF REGIONAL ANESTHESIA (WWW.NYSORA.COM)

EO – external oblique

IO – internal oblique

TA -transversus abdominis

2.4 Indications of TAP block

TAP block was shown to reduce the need for postoperative opioid use, increase the time to first request for further analgesia, and provide more effective pain relief, while decreasing opioid related side effects such as sedation and postoperative nausea and vomiting.

Studies included a combination of both general abdominal and gynaecologic procedures. The introduction of ultrasound has allowed providers to identify the appropriate tissue plane and perform this block with greater accuracy under direct visualization.

TAP block is simple procedures that can be used as an adjunct for postoperative pain control in abdominal, gynaecologic, or urologic surgery involving the T6 to L1 distribution. Surgical procedures investigated by randomized clinical trials include large bowel resection, caesarean abdominal hysterectomy, open appendectomy, and laparoscopic cholecystectomy.

However, TAP block has also found clinical utility in procedures such as abdominal and inguinal hernia repair, radical prostatectomy, nephrectomy and many different laparoscopic procedures in general.

Bilateral TAP blocks can be used for midline incisions. This technique is also useful for procedures in which epidural analgesia is contraindicated (i.e., anticoagulated patients). In addition, if prolonged analgesia is desired, a continuous TAP block technique with placement of a catheter has been described.

2.5 Contraindications

Very few contraindications exist to performing a TAP block. Absolute contraindications include infection at the site of injection, patient refusal or inability to cooperate, and allergy to local anaesthetics.

2.6 Monitoring the analgesic effectiveness

This includes assessing:

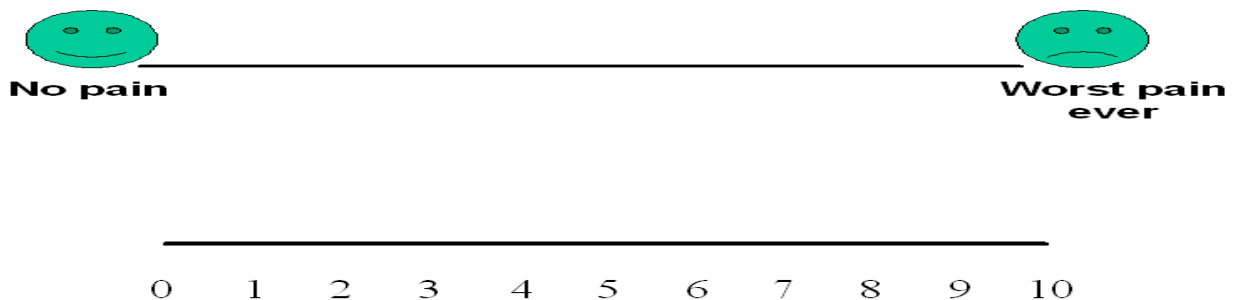
- Pain intensity
- Pain relief
- Functionality and rehabilitation
- Adverse effects.

2.6.1 National Initiative on Pain Control

The National Initiative on Pain Control™ (NIPC™) has provided diagnostic tools to assist in assessing the severity and quality of pain experienced by patients [11]

2.6.2 Visual Analog Scale

A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. It is a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in millimetres from the left hand end of the line to the point that the patient marks.



2.6.3 Verbal Pain Intensity Scale

No pain

Mild pain

Moderate pain

Severe pain

Very severe pain

Worst pain possible

Anne Marie Sorce, *Pain Assessment Scales.*, 2005.

2.7 Efficacy of TAP block

There have been a number of randomized controlled trials comparing the efficacy of TAP block to that of local anaesthetic infiltration with varying results.

Ranjit et al [12] compared the analgesic efficacy of TAP block with local bupivacaine infiltration in patients undergoing gynaecological surgeries with Pfannenstiel incision and lower midline incision under general anaesthesia. Patients were randomly allocated to three groups: control group (n=15), TAP block group (n=15), with 0.25% bupivacaine, and local infiltration group with 0.25% bupivacaine at the end of surgery. They all received intramuscular diclofenac 12 hourly and intravenous tramadol in the postoperative period. Visual analogue scores for pain were assessed at 1, 2, 4, 8, 12 and 24 hours postoperatively and average tramadol consumption in 24 hours. Visual analogue scores were significantly less in TAP block group and effect lasted up to 12 hours at rest postoperatively and 8 hours during cough and movement and thus concluded that bilateral TAP block was effective in reducing postoperative pain scores for 8 to 12 hours postoperatively and opioid requirement.

Nanze Yulet et al [13] conducted a meta-analysis of randomized controlled trials to compare the efficacy of single shot TAP block with that of single shot LAI for postoperative

analgesia in adults after lower abdominal surgeries. Major medical databases and trial registries were searched for published and unpublished RCTs. They evaluated postoperative visual analogue scale (VAS) pain score, morphine requirement, and rate of postoperative nausea and vomiting (PONV). Four RCTs, encompassing 96 TAP-block and 100 LAI patients, were included in the final analysis. Patients in the TAP-block group had lower VAS pain scores 24 hours postoperatively compared with the LAI group, both at rest and with movement. There were no significant between-group differences in 24-hour postoperative morphine requirements, the rates of PONV or VAS pain scores at 2 and 4 h postoperatively. They concluded that TAP block and LAI provide comparable short-term postoperative analgesia, but TAP block has better long-lasting effect.

Atim et al [14] carried out a prospective, double-blind randomized controlled study to evaluate the efficacy of ultrasound guided transversus abdominis plane (TAP) block and bupivacaine infiltration of the skin and subcutaneous tissue of the wound in patients undergoing hysterectomy. Patients were randomly allocated to three groups: a control group (n = 18) and TAP block group (n = 18) received bilateral TAP blocks with saline and bupivacaine respectively, and an infiltration group (n = 19) received skin and subcutaneous wound tissue infiltration with bupivacaine at the end of surgery. They all received patient-controlled intravenous tramadol and were assessed for pain and tramadol consumption at 1, 2, 4, 6 and 24 hours. Both the TAP and infiltration groups had lower movement and rest pain scores than the control group, with lower scores in the TAP group than the infiltration group at 6 and 24 hours. Total tramadol consumption was significantly lower in the TAP group than in the other groups at all-time points. They concluded that ultrasound-guided TAP block reduced rest and movement pain after total abdominal hysterectomy and was more effective than superficial wound infiltration for postoperative pain management.

Vijayalakshmi et al [15] carried out a prospective randomized controlled trial to compare the analgesic efficacy of transversus abdominis plane block with that of direct infiltration of local anaesthetic into surgical incision in lower abdominal procedures. ASA I-II patients undergoing lower abdominal gynaecological procedures under general anaesthesia were divided randomly into two groups. A bilateral TAP block with 0.25% bupivacaine 0.6 ml/kg was performed on one group and local infiltrate after skin closure with the same amount of drug on the other group. Intravenous patient controlled analgesia system with morphine for 24 hours was administered on all patients. The time taken for the first rescue analgesic and visual analog score (VAS) and 24-hour morphine requirement and sedation scores were assessed. They concluded that TAP block is an effective means of analgesia for lower abdominal surgeries with minimal side effects.

Pernille et al [16] carried out a randomized and double-blind study to evaluate the analgesic effect of a TAP block in patients scheduled for primary inguinal hernia repair. The TAP block was evaluated versus placebo and ilioinguinal block and wound infiltration. Ninety patients were allocated to one of three groups: group TAP, group infiltration (ilioinguinal nerve block and wound infiltration) and group placebo. Visual analogue pain scores while coughing and at rest demonstrated no difference between groups. Pain scores at 6h were significantly lower in-group infiltration than in group TAP and placebo at rest, Median morphine consumption was lower in-group infiltration than in-group placebo. They concluded that ultrasound-guided TAP block did not reduce postoperative pain after inguinal hernia repair.

El Hachem et al [17] carried out a randomized double blinded clinical trials to evaluate efficacy of TAP block versus trocar site infiltration of bupivacaine in gynaecological laparoscopic surgeries in reducing post-operative pain control. Women undergoing

gynaecologic laparoscopy using a 4-port symmetrical technique were randomly assigned to right- or left-sided TAP block using 30 mL of 0.25% bupivacaine with epinephrine. Two cohorts of patients were studied. Cohort 1 consisted of anaesthesiologist-administered ultrasound-guided TAP block and cohort 2 consisted of surgeon-administered laparoscopic-guided TAP block. In both cohorts, contralateral port sites were infiltrated with an equal amount of bupivacaine in divided doses. All patients received intraoperative acetaminophen and ketorolac. Postoperative abdominal pain was assessed at 1, 2, 4, 6, 8, 12, 18, 24, and 48 hours on the block and contralateral sides, before and after palpation, using the 10 point visual analog scale. Neither block method provided a significant clinical benefit compared with trocar site bupivacaine infiltration.

Marais et al [18] evaluated the postoperative analgesic efficacy of bilateral ultrasound-guided TAP blocks, in patients undergoing total abdominal hysterectomy using a prospective, randomized, double-blind, controlled study. Thirty patients were allocated to two groups; a TAP block group (n = 15) and a placebo group (n = 15). The TAP blocks were performed with 0.25% bupivacaine. The placebo group received blocks with normal saline, post induction of anaesthesia. All patients received patient-controlled intravenous morphine for analgesia post operatively. Morphine consumption during the first 24 hours and pain scores at 0, 6 and 24 hours postoperatively were assessed and concluded that bilateral ultrasound-guided TAP blocks significantly reduced postoperative morphine consumption.

Bamigboye et al [19] sought to determine the efficacy of local anaesthetic wound infiltration for postoperative pain relief in caesarean section concluded that local anaesthetic infiltration and abdominal nerve blocks are of benefit in CS by reducing opioid consumption

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Research Design

The study adopted an observational study design. It is a valuable and effective approach to determine associations between specific exposures and outcomes [24,25].

3.2 Study Area and Target Population

The study was conducted at Kenyatta National Hospital main theatre among adult women undergoing elective pelvic gynaecological surgery for a period of 3 months from December 2017 to February 2018.

3.3 Exclusion and inclusion criteria

3.3.1 Inclusion criteria

The study included consenting patients who fulfilled the following characteristics.

- ASA 1 and 2 patients scheduled for elective gynecological pelvic surgery
- BMI (18.5-30)
- Admitted patients undergoing pelvic gynecological surgery

3.3.2 Exclusion criteria

- Children
- ASA 3 and 4
- Emergency gynecological pelvic surgery
- Procedures done under regional anaesthesia
- Patients who declined consent to the study and administration of TAP block

- Patients allergic to local anesthetics

3.4 Sample Size Determination and Sampling Procedure

3.4.1 Sample Size Determination

Being a one-arm study, the sample size was determined using the Fisher formula given by:

$$n_0 = \frac{z^2 \times p \times (1-p)}{d^2} = \frac{1.96^2 \times 0.5 \times (1-0.5)}{0.05^2} = 384.16 \approx 384$$

Where n_0 = initial sample size

z = value of z corresponding to alpha/ absolute precision (0.05%)

p = prevalence of patients on TAP block (50%)

d = margin of error

$$n = \frac{n_0}{1 + \frac{n_0 - 1}{N}} = \frac{384}{1 + \frac{384 - 1}{48}} = 42.8 \approx 43$$

3.4.2 Sampling Procedure

Consecutive non-randomized sampling was applied whereby every patient who fit the inclusion criteria and consented to the study was recruited in the morning of the procedure in theatre.

3.5 Study procedure

Patient was educated on post-operative pain and its management, interpretation and filling of the pain assessment tools, TAP block procedure, its benefits and risks.

Patient received general anaesthesia as per the provider's preference. Which included the combinations below

- Fentanyl at induction 1-2mcg per Kg IV
- Paracetamol 10-15mg per Kg IV
- Morphine 0.05-0.1mg/Kg IV
- Diclofenac 0.5-1mg/Kg IM/PR
- 20cc of 0.25% plain bupivacaine bilateral TAP blocks at the end of the procedure before reversal of the patient

Post-operative pain management

- Paracetamol PO 10-15mg/Kg
- Diclofenac PR/PO 0.5mg/kg
- Tramadol IV 1-2mg/kg
- Morphine 0.05-0.1mg/Kg PRN

Equipment

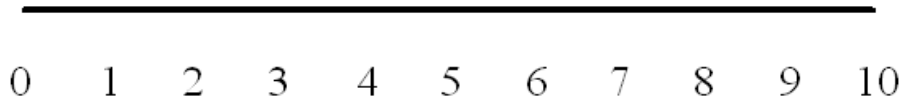
- Ultrasound machine with a high frequency probe(10- 15 MHz)
- Ultrasound probe cover
- Antiseptic for skin disinfection
- Sterile ultrasound gel
- Needle 50mm or 80mm
- 20mls needle and injection tubing
- 20mls 0.25% bupivacaine

Patient in supine position, ultrasound probe placed in a transverse plane between the lower coastal margin and the iliac crest in mid axillary line.

Needle was advanced using in plane technique with an anteromedial to posteromedial direction between the aponeurosis of the internal oblique and transversus abdominis muscle.

3.6 Operational Definitions

Visual analogue pain scores were used:



0 no pain

1-3 mild pain

4-6 moderate pain

7-9 severe pain

10 very severe pain

Success of the block was determined by correct placement of the local anaesthetic in the plane between internal oblique and transversus abdominis as visualized under ultrasound.

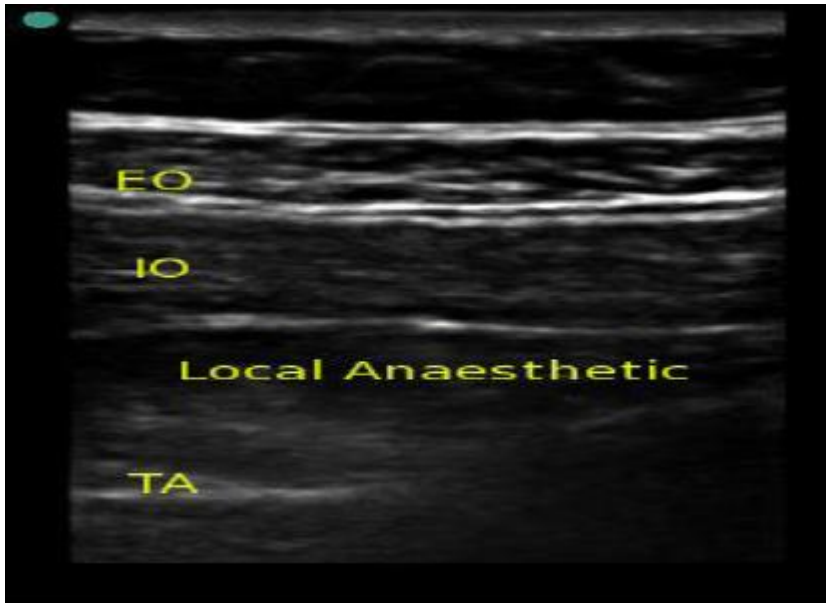


Figure 4: Correct local anaesthetic deposition in the transversus abdominis plane

EO – External oblique

IO – Internal oblique

TA – Transversus abdominis

3.7 Data Collection Procedure

The data was collected using a survey questionnaire administered to the patient by the trained research assistant.

3.8 Data Analysis

Data analysis was done using SPSS (Statistical Package for the Social Sciences) vs 20. Descriptive statistics such as mean, median and measures of dispersion, frequencies and percentages were used to describe the pain scores, analgesia requirements and time to ambulation. Findings are also presented in the form of text, charts, graphs and tables.

3.9 Ethical Considerations

Permission to conduct the research was sought from Kenyatta National Hospital and University of Nairobi Ethical and Research Committee.

The participants were provided with information on the research and its intended purpose and informed consent was obtained from them.

CHAPTER FOUR: STUDY RESULTS

4.1 Demographic characteristics

The study to determine the analgesic effectiveness of single-shot ultrasound guided TAP block after pelvic gynaecological surgeries at KNH in the first 24 hours used a sample of 45 patients.

The mean age of the patients was 41.2 with a range between 26 and 69 years and a larger proportion 21(46.7%) aged 36 to 45 years (Table 1). The age was distributed as indicated in Figure 5 below.

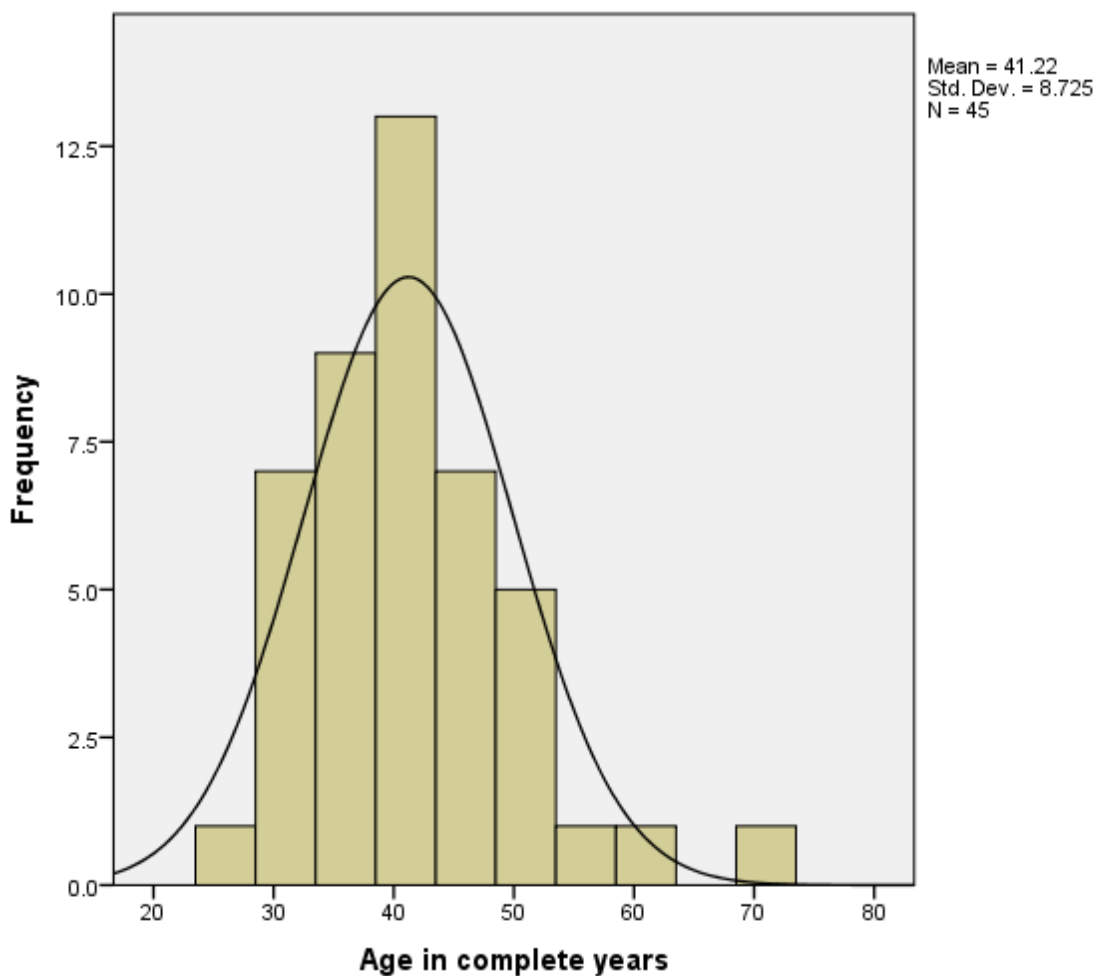


Figure 5: Distribution of age in years

A section of 18(40%) had completed secondary education while 11(24.4%) had tertiary education, Table 1.

Table 1: Demographic characteristics

Demographic variable	Categories	Frequency	Percent	Median	p-value
Age groups (years)	26-35	13	28.9	2 (36-45 years)	<0.01
	36-45	21	46.7		
	46-55	8	17.8		
	56-65	2	4.4		
	66-75	1	2.2		
Level of education	None	1	2.2	4 (Secondary school)	0.01
	Primary school-incomplete	4	8.9		
	Primary school	9	20.0		
	Secondary school-incomplete	2	4.4		
	Secondary school	18	40.0		
	Diploma	2	4.4		
	Tertiary	3	6.7		
	College	6	13.3		

4.2 BMI

A greater section of (62.7%) patients were overweight, Table 4.2.

Table 2: BMI

BMI	Frequency	Percent	Median	p-value
Normal	11	21.5	5 (Overweight)	<0.01
Overweight	32	62.7		
Obese Class	8	15.6		

The distribution of the BMI was as shown in Figure 6 below.

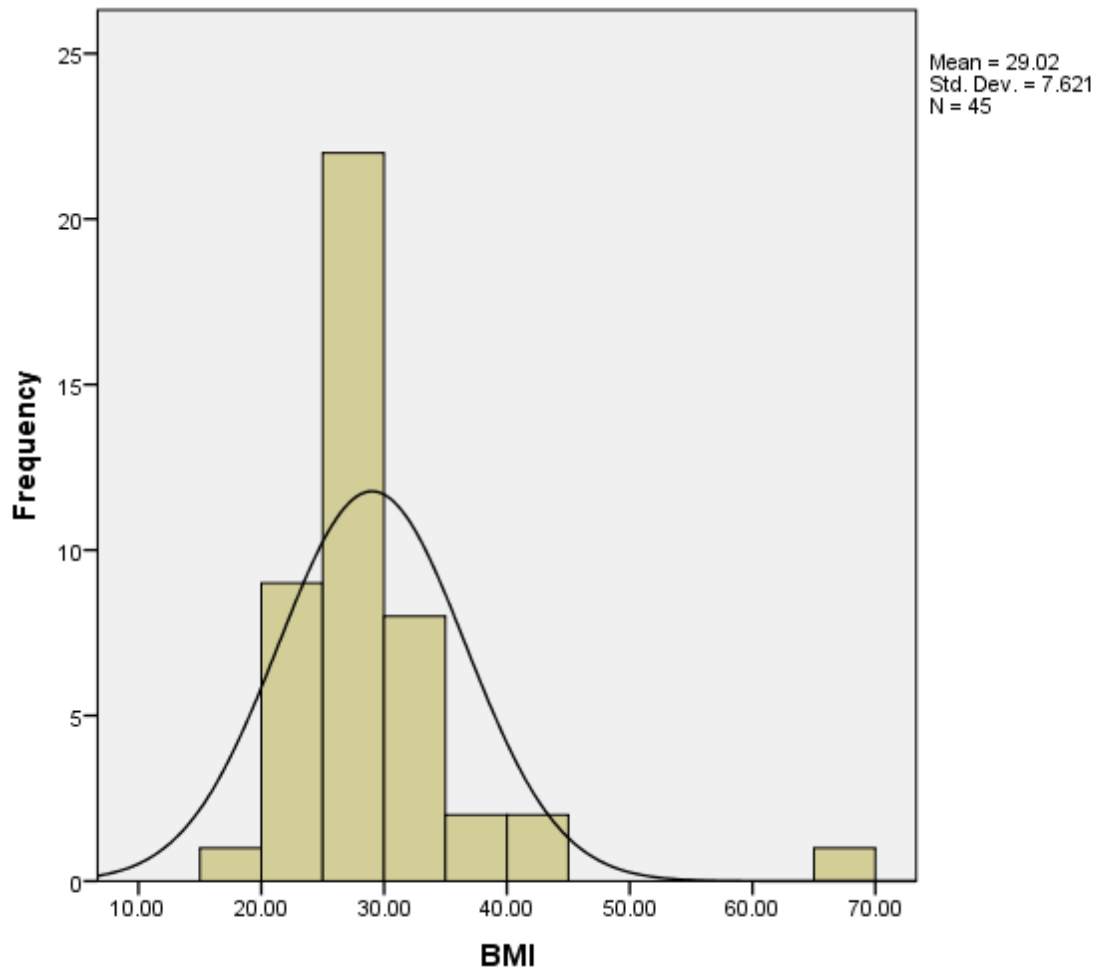


Figure 6: BMI Distribution

4.3 Type of pelvic gynaecological surgery

The main pelvic gynaecological surgery was TAH 26(57.8%). There was no significant difference in the distribution of patients administered on myomectomy and TAH surgeries (p-value=0.371), Table 3.

Table 3: Type of pelvic gynaecological surgery

Type of pelvic gynaecological surgery	Frequency	Percent	Median	p-value
Myomectomy	19	42.2	42.2	0.371
TAH	26	57.8		

4.4 Indication for the surgery

The main indication for the surgery was Fibroids 33(73.3%), Table 4.

Table 4: Indication for the surgery

Indication for the surgery	Frequency	Percent	Median	p-value
Fibroids	33	73.3	73.3	<0.01
Endometrial lesion	3	6.7		
Cervical lesion	3	6.7		
Ovarian lesion	6	13.3		

4.5 Induction drugs

The combination of induction drugs used by many providers was Fentanyl + Propofol + Cisatracurium, Table 5 below.

Table 5: Induction drugs

Induction drugs	Frequency	Percent	Median	p-value
Fentanyl + Propofol + Atracurium	14	24.4	2 (Fentanyl + Propofol + Cisatracurium)	<0.01
Fentanyl + Propofol + Cisatracurium	19	37.8		
Fentanyl + Propofol + Sux +Atracurium	2	4.4		
Fentanyl + Propofol + Midazolam	2	4.4		
Fentanyl + Propofol + Atracurium + Dexmedetomidine	2	4.4		
Fentanyl + Propofol + Midazolam + Atracurium	1	2.2		
Fentanyl + Propofol + Cisatracurium + Sux	2	4.4		
Fentanyl + Propofol + Atracurium + Cisatracurium	1	2.2		
Fentanyl + Propofol + Cisatracurium + Midazolam	3	2.2		

4.6 Maintenance/ Analgesia

The most used combination of maintenance Analgesia drugs was Morphine + Diclofenac, Table 6 below.

Table 6: Maintenance/ Analgesia drugs

Maintenance/ Analgesia	Frequency	Percent	Median	p-value
Morphine + Diclofenac	30	66.7	1 (Morphine + Diclofenac)	<0.01
Morphine + Diclofenac + Paracetamol	8	17.8		
Morphine + Diclofenac + Remifentanyl	3	6.7		
Morphine + Diclofenac + Paracetamol + Dexmedetomidine	1	2.2		
Paracetamol + Dexmedetomidine	2	4.4		
Paracetamol +Morphine	1	2.2		

4.7 Blood pressure

Systolic blood pressure decreased at an average of 2.04% between the pre-operative and intra operative readings, and a rise noted at an average of 2.79% post-operatively.

Diastolic blood pressure reduced at an average of 5.49% between pre-operative and intra operative readings and increased at an average of 7.26% post-operatively,

Table 7.

Table 7: Blood pressure percentage changes

Time	Change	Minimum	Maximum	Mean	Std. Error	Std. Deviation
Pre-operative – Intra operative	Systolic	-40.54	343.33	2.0442	7.94357	53.28706
Intra operative - Post operative	Systolic	-38.57	300.00	2.7872	7.08180	47.50615
Pre-operative – Intra operative	Diastolic	-39.18	60.00	-5.4941	2.93303	19.67536
Intra operative - Post operative	Diastolic	-83.33	62.07	-7.2613	3.50817	23.53354

4.8 Heart Rate

Heart rate increased at an average of 1.73% intra operatively. Heart rate reduced at an average of 2.21% post operatively, Table 8.

Table 8: Heart Rate change in percentage

Heart Rate	Minimum	Maximum	Mean	Std. Error	Std. Deviation
Pre-operative – Intra operative	-33.90	23.75	1.7296	1.87630	12.58659
Intra operative - Post operative	-94.62	34.78	-2.2126	3.05966	20.52484

4.9 Post-operative pain management

Table 9: Post-operative pain analgesia combination

Postoperative pain management	Frequency	Percent	Median	p-value
Betapyn	1	2.2	2.2	<0.01
Diclofenac	3	6.7		
Morphine + Tramadol	6	13.3		
Diclofenac + Morphine	6	13.3		
Diclofenac + Paracetamol	6	13.3		
Diclofenac + Tramadol	1	2.2		
Diclofenac + Pethidine	1	2.2		
Morphine + Diclofenac + Paracetamol	15	33.3		
Diclofenac + Tramadol + Morphine	1	2.2		
Diclofenac + Pethidine + Morphine	2	4.4		
Diclofenac + Pethidine + Paracetamol	3	6.7		

4.10 Anaesthesia providers

Registrars were the main 31(68.9%) anaesthesia providers who performed the TAP block, Table 10.

Table 10: Anaesthesia providers

Anaesthesia providers	Frequency	Percent	Median	p-value
Consultant	14	31.1	31.1	0.017
Registrar	31	68.9	68.9	

4.11 Pain scores

The overall average pain score was 2.138(mild pain), Table 11.

Table 11: Pain scores

Time of pain observation	Minimum	Maximum	Mean score	Std. Error	Std. Deviation
Immediately	0	6	2.58	.205	1.373
After 6 hours	0	6	2.38	.197	1.319
After 12 hours	0	6	2.11	.206	1.368
After 18 hours	0	6	1.95	.179	1.174
After 24 hours	0	6	1.67	.181	1.132
Overall mean			2.138	0.1936	1.2732

4.12 Time to request analgesia

The average time to first request for analgesia was 9hours.33 patients requested for analgesia 15 were given tramadol 9 morphine and 6 paracetamol .3 were not given.12 patients did not request for analgesia.

Table 12: Time to request analgesia

Time to request analgesia	Minimum	Maximum	Mean	Std. Error	Std. Deviation
First	0	1440	494.38	73.296	463.566
Second	360	1440	990.00	226.495	452.990

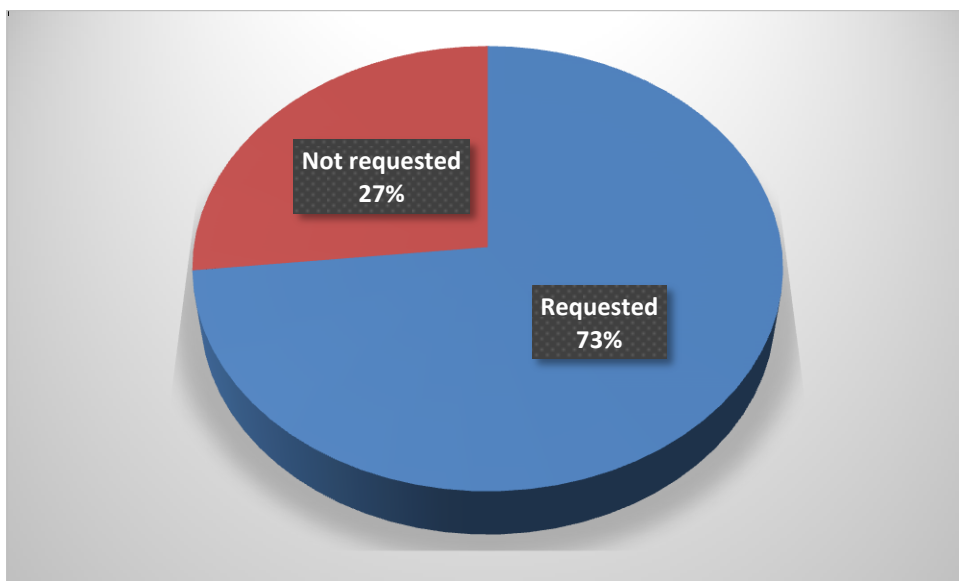


Figure 7: Requested vs unrequested (a)

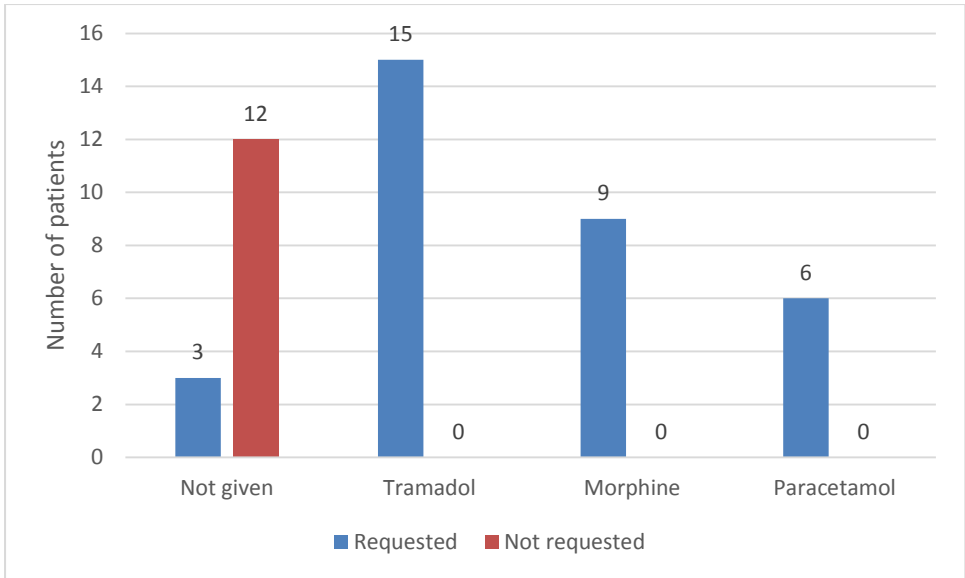


Figure 8: Requested vs unrequested (b)

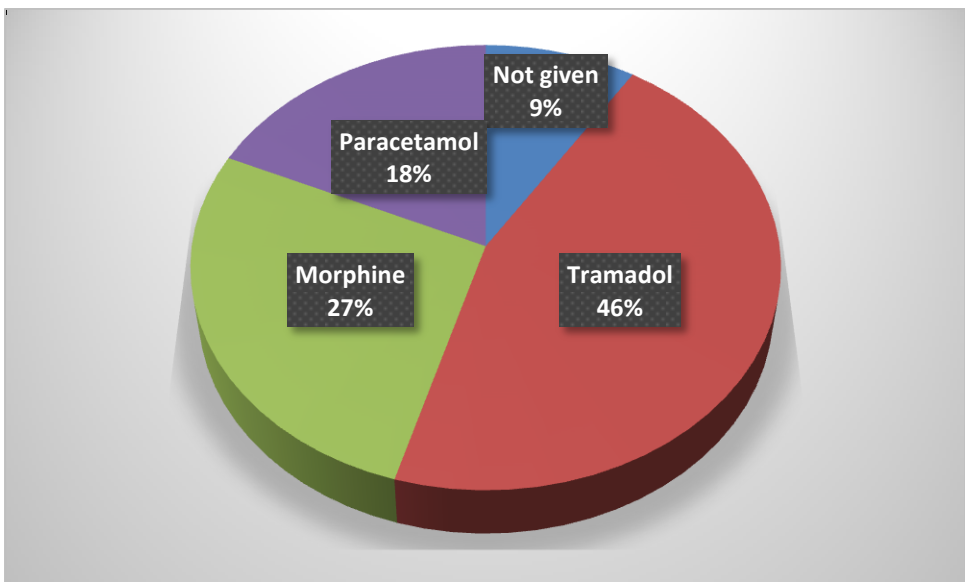


Figure 9: Requested vs unrequested (c)

4.13 Time to ambulation

The average time to ambulation was 18 hours Table 13.

Table 13: Time of ambulation

Minimum	Maximum	Mean	Std. Error	Std. Deviation
360	1440	1056.00	36.898	247.519

4.14 Complications

Blood loss was reported in one patient. Nausea was the most experienced post-operative event, Table 14.

Table 14: Post-operation events

Post-operation events	Frequency	Percent
Nausea	16	35.6
Vomiting	7	15.6
Diarrhoea	1	2.2

4.15 Relationship between Pain scores and maintenance combination analgesia

The relationship between pain scores and maintenance analgesia combination was not significant (p-value=0.665).

4.16 Relationship between Pain scores and post-operative management

The relationship between pain scores and post-operative analgesia combination given was not significant (p-value=0.665).

CHAPTER FIVE: DISCUSSION

5.1 Discussion

45 Patients received bilateral TAP blocks with 20mls 0.25% bupivacaine after pelvic gynaecological surgeries and followed up at 0,6,12,18,24hours post operatively.

On the demographic characteristics the mean age of the patients was 41.2 with a range between 26 and 69 years and a larger proportion 21(46.7%) aged 36 to 45 years (Table 1). It was a normal distribution curve and so a good representation of the population. A section of them 18(40%) had completed secondary education while 11(24.4%) had tertiary education and thus most of them understood the study easily and were able to give objective scores of their pain. (62.7%) patients were overweight with BMI of between (25.0 and 29.9) with a normal distribution curve which also gave a representation of the general population.

The main pelvic gynaecological surgery was TAH 26(57.8%) with the main indication for the surgeries being fibroids 33(73.3%).There was no significant difference in the distribution of patients administered on myomectomy and TAH surgeries (p-value=0.371)

The combination of induction drugs used by most of the providers was Fentanyl + Propofol + Cisatracurium, with maintenance Analgesia drugs of Morphine + Diclofenac and postoperative analgesia being Morphine+Diclofenac and paracetamol.This were noted to be the analgesics that were easily available in the hospital at the time of this study.However the relationship between pain scores and maintenance analgesia and post operative analgesia combination was not significant (p-value=0.665).

Heart rate increased at an average of 1.73% intra operatively and reduced at an average of 2.21% post operatively. Systolic blood pressure decreased at an average of 2.04% between the pre-operative and intra operative readings, and a rise noted at an average of 2.79% post-operatively. Diastolic blood pressure reduced at an average of 5.49% between pre-operative and intra operative readings and increased at an average of 7.26% post-operatively. However, the changes were not significant.

The overall average pain score was 2 (mild pain) and the average time to request analgesia was 9 hours post operatively. 12 patients did not request for rescue analgesia therefore reducing their opioid requirements. 33 patients requested for analgesia 15 were given tramadol 9 morphine and 6 paracetamol. 3 were not given.

Nausea, Vomiting and Diarrhoea were the side effects experienced post operatively, they are more likely to be attributed to the anaesthetics and analgesics given.

These results are comparable to a study done by Ranjit et al [12] which compared the analgesic efficacy of TAP block with local bupivacaine infiltration in patients undergoing gynaecological surgeries with Pfannenstiel incision and lower midline incision under general anaesthesia. Patients were randomly allocated to three groups: control group (n=15), TAP block group (n=15), with 0.25% bupivacaine, and local infiltration group with 0.25% bupivacaine at the end of surgery. They all received intramuscular diclofenac 12 hourly and intravenous tramadol in the post operative period. Visual analogue scores for pain were assessed at 1, 2, 4, 8, 12 and 24 hours postoperatively and average tramadol consumption in 24 hours. Visual analogue scores were significantly less in TAP block group and effect lasted up to 12 hours at rest postoperatively and 8 hours during cough and movement and thus concluded that bilateral TAP block was effective in reducing postoperative pain scores for 8 to 12 hours postoperatively and opioid requirement.

In a similar study, Atim et al [14] carried out a prospective, double-blind randomized controlled study to evaluate the efficacy of ultrasound guided transversus abdominis plane (TAP) block and bupivacaine infiltration of the skin and subcutaneous tissue of the wound in patients undergoing hysterectomy. Patients were randomly allocated to three groups: a control group (n = 18) and TAP block group (n = 18) received bilateral TAP blocks with saline and bupivacaine respectively, and an infiltration group (n = 19) received skin and subcutaneous wound tissue infiltration with bupivacaine at the end of surgery. They all received patient-controlled intravenous tramadol and were assessed for pain and tramadol consumption at 1, 2, 4, 6 and 24 hours. Both the TAP and infiltration groups had lower movement and rest pain scores than the control group, with lower scores in the TAP group than the infiltration group at 6 and 24 hours. Total tramadol consumption was significantly lower in the TAP group than in the other groups at all-time points. They concluded that ultrasound-guided TAP block reduced rest and movement pain after total abdominal hysterectomy and was more effective than superficial wound infiltration for postoperative pain management.

Vijayalakshmi et al [15] also carried out a prospective randomized controlled trial to compare the analgesic efficacy of transversus abdominis plane block with that of direct infiltration of local anaesthetic into surgical incision in lower abdominal procedures. ASA I-II patients undergoing lower abdominal gynaecological procedures under general anaesthesia were divided randomly into two groups. A bilateral TAP block with 0.25% bupivacaine 0.6 ml/kg was performed on one group and local infiltrate after skin closure with the same amount of drug on the other group. Intravenous patient controlled analgesia system with morphine for 24 hours was administered on all patients. The time taken for the first rescue analgesic and visual analog score (VAS) and 24-hour morphine requirement and sedation

scores were assessed. They concluded that TAP block is an effective means of analgesia for lower abdominal surgeries with minimal side effects.

Marais et al [18] evaluated the postoperative analgesic efficacy of bilateral ultrasound-guided TAP blocks, in patients undergoing total abdominal hysterectomy using a prospective, randomized, double-blind, controlled study. Thirty patients were allocated to two groups; a TAP block group (n = 15) and a placebo group (n = 15). The TAP blocks were performed with 0.25% bupivacaine. The placebo group received blocks with normal saline, post induction of anaesthesia. All patients received patient-controlled intravenous morphine for analgesia post operatively. Morphine consumption during the first 24 hours and pain scores at 0, 6 and 24 hours postoperatively were assessed and concluded that bilateral ultrasound-guided TAP blocks significantly reduced postoperative morphine consumption.

The average time to complete ambulation when the patient would comfortably be up and about without much strain and pain was noted to be 18 hours. Adequate rest and movement pain management post operatively reduces length of hospital stay and risks of DVT. Pelvic gynaecological surgeries are among the surgeries with an increased risk of DVT as shown by a study by Anderson FA Jr., Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. *Arch Intern Med.* 1991;151:933–938.

Registrars were the main 31(68.9%) anaesthesia providers who performed the TAP block because they were covering their rotation in that theatre daily and the consultants were overseeing.

5.2 Conclusion

Single shot ultrasound guided TAP block after pelvic gynaecology surgeries in combination with conventional analgesia is effective in reducing pain scores for 8 to 12hrs post operatively, reduction of opioid requirement and also rest and movement pain encouraging early ambulation with minimal side effects.

5.3 Recommendations

Routine use of ultrasound guided TAP block in combination with conventional analgesia in pelvic gynaecological surgeries for post operative pain management.

Acquire ultrasound machine and other necessary equipment necessary for **TAP block**.

Randomized Control Trial to compare the effectiveness of post operative pain control between the conventional analgesics and the **TAP block**.

5.4 Limitations

Lack of standardisation of the perioperative and intraoperative analgesia regimen since it was done by different anaesthesia providers who used their preference.

Ultrasound machine was not readily available for every anaesthesia provider who wished to perform the block.

APPENDICES

REFERENCES

- [1] C. I. Ripamonti, "Pain management," *Annals of Oncology*, vol. 23, no. 10, pp. x294-x301, 2012.
- [2] Nalini Vadivelu, Sukanya Mitra, and Deepak Narayan, "Recent Advances in Postoperative Pain Management," *Yale Journal of Biology and Medicine*, vol. 83, no. 1, pp. 11–25, 2010.
- [3] Selvi K. Kumar, "Intravenous Acetaminophen use in Postoperative Pain Management," Rhode Island College, Master's Thesis 2014.
- [4] Alban Latremoliere and Clifford J. Woolf, "Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity," *J Pain*, vol. 10, no. 9, pp. 895–926, 2009.
- [5] Lihua Zhang, Xiancui Liu, and Yunxia Xue, "Analysis of deep venous thrombosis after Gynecological surgery: A clinical study of 498 cases," *Pakistani Journal of Medical Science*, vol. 31, no. 2, pp. 453–456., 2015.
- [6] M. H. Andreae and D. A. Andreae, "Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis," *British Journal of Anaesthesia*, 2013.
- [7] Karim Mukhtar, "Transversus Abdominis Plane (TAP) Block ," *The Journal Of The New York School Of Regional Anesthesia*, vol. 12, pp. 28-33, 2009.
- [8] Kathryn L. McCance and Sue E. Huether, *Pathophysiology: The Biologic Basis for Disease in Adults and Children.*: Elsevier Health Sciences, 2013.
- [9] Mark J. Young, Andrew W. Gorlin, Vicki E. Modest, and Sadeq A. Quraishi, "Clinical Implications of the Transversus Abdominis Plane Block in Adults," *Anesthesiology Research and Practice*, vol. 2012, p. 731645, 2012.
- [10] Nanze Yu et al., "Transversus abdominis-plane block versus local anesthetic wound infiltration in lower abdominal surgery: a systematic review and meta-analysis of randomized controlled trials," *BMC Anesthesiol.*, vol. 14, no. 121, 2014.
- [11] Anne Marie Sorce, *Pain Assessment Scales.*, 2005.
- [12] Ranjit S and Shrestha SK, "Comparison of ultrasound guided transversus abdominis plane block versus local wound infiltration for post operative analgesia in patients undergoing gynaecological surgery under general anaesthesia.," *Kathmandu Univ Med J (KUMJ)* . , vol. 12, no. 46, pp. 93-96, 2014.
- [13] N Yu et al., "Transversus abdominis-plane block versus local anesthetic wound infiltration in lower abdominal surgery: a systematic review and meta-analysis of randomized controlled trials.," *BMC Anesthesiol.*, vol. 14, no. 121, 2014.
- [14] A Atim et al., "The efficacy of ultrasound-guided transversus abdominis plane block in patients undergoing hysterectomy," *Anaesth Intensive Care.*, vol. 39, no. 4, pp. 630-634, 2011.
- [15] Vijayalakshmi Sivapurapu, Arumugam Vasudevan, Sumanlata Gupta, and Ashok S

- Badhe, "Comparison of analgesic efficacy of transversus abdominis plane block with direct infiltration of local anesthetic into surgical incision in lower abdominal gynecological surgeries," *Journal of Anaesthesiology Clinical Pharmacology*, vol. 29, no. 1, pp. 71-75, 2013.
- [16] PL Petersen et al., "The effect of transversus abdominis plane block or local anaesthetic infiltration in inguinal hernia repair: a randomised clinical trial.," *Eur J Anaesthesiol.*, vol. 30, no. 7, pp. 415-421, 2013.
- [17] L El Hachem et al., "Randomized controlled double-blind trial of transversus abdominis plane block versus trocar site infiltration in gynecologic laparoscopy.," *Am J Obstet Gynecol.*, vol. 12, no. 2, p. 182, 2015.
- [18] Adri Marais, Owen Porrill, M F James, and Robert Dyer, "The use of ultrasound-guided transversus abdominis plane blocks for total abdominal hysterectomy: a double-blind, controlled trial," *South African Journal of Anaesthesia and Analgesia*, vol. 20, no. 2, 2014.
- [19] Anthony Akinloye Bamigboye and George Justus Hofmey, "Caesarean section wound infiltration with local anaesthesia for postoperative pain relief - any benefit?," *South African medical journal*, vol. 100, no. 5, pp. 313-319, 2010.
- [20] Mohammad Zohrabi, "Mixed Method Research: Instruments, Validity, Reliability and Reporting Findings," *Theory and Practice in Language Studies*, vol. 3, no. 2, pp. 254-262, February 2013.
- [21] Edward L. Hannan, "Randomized Clinical Trials and Observational Studies: Guidelines for Assessing Respective Strengths and Limitations," *JACC: Cardiovascular Interventions*, vol. 1, no. 3, pp. 211–217, 2008.
- [22] Mariana Chavez-MacGregor and Sharon H. Giordano, "Randomized Clinical Trials and Observational Studies: Is There a Battle?," *Journal of Clinical Oncology*, pp. 1-4, 2016.
- [23] Matthew S. Thiese, "Observational and interventional study design types; an overview," *Biochemia Medica*, vol. 24, no. 2, pp. 199-210, 2014.
- [24] Alessandro Wasum Mariani and Paulo Manuel Pêgo-Fernandes, "Observational studies: why are they so important?," *Sao Paulo Medical Journal*, vol. 132, no. 1, 2014.
- [25] Demetra Daskalos Logothetis, "Anesthetic Buffering: New Advances for Use in Dentistry," 2013.
- [26] Mayank Gupta and Robert Goodson, "Transverse Abdominal Plane Neurostimulation for Chronic Abdominal Pain: A Novel technique," *Pain Physician*, vol. 17, pp. 619-622, 2014.
- [27] G. McDermott et al., "Should we stop doing blind transversus abdominis plane blocks?," *British Journal of Anaesthesia*, vol. 108, no. 3, pp. 499-502, 2012.
- [28] T. G. Egziabher, J. Ruminjo, and C. Sekadde-Kigonde, "Pain Relief Using Paracervical Block In Patients Undergoing Manual Vacuum Aspiration Of Uterus," *East African Medical Journal*, vol. 79, no. 10, pp. 530-534, 2002.

[29] Anderson FA Jr., Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. *Arch Intern Med.* 1991;151:933–938.