PREVALENCE OF POST MASTECTOMY PAIN SYNDROME
AT KENYATTA NATIONAL HOSPITAL

A DISSERTATION SUBMITTED IN PART FULFILLMENT OF THE
REQUIREMENTS FOR AWARD OF THE DEGREE OF MASTER OF MEDICINE
(ANAESTHESIA) OF THE UNIVERSITY OF NAIROBI

DR. IRAYA A. MUNGAI
NOVEMBER 2017
PRINCIPAL INVESTIGATOR

**DR IRAYA ANTHONY MUNGAI, MBChB (UON)**

POST GRADUATE STUDENT IN ANAESTHESIOLOGY,
DEPARTMENT OF ANAESTHESIA,
UNIVERSITY OF NAIROBI

SUPERVISORS

**DR THOMAS M. CHOKWE, BSc Anatomy, MBChB, Mmed Anaesthesia (UON)**
LECTURER IN ANAESTHESIOLOGY AND CRITICAL CARE MEDICINE
DEPARTMENT OF ANAESTHESIA,
UNIVERSITY OF NAIROBI

**DR MWITI T. MURIITHI, MBChB (MOI), Mmed Anaesthesia (UON), Fellow Pain Management**
LECTURER IN ANAESTHESIOLOGY AND PAIN SPECIALIST
DEPARTMENT OF ANAESTHESIA,
UNIVERSITY OF NAIROBI

**DR GATHERU K. ANTONY, MBChB, Mmed Anaesthesia (UON)**
LECTURER IN ANAESTHESIOLOGY
DEPARTMENT OF ANAESTHESIA,
UNIVERSITY OF NAIROBI
DECLARATION

Candidate’s declaration
I hereby declare that this dissertation is my original work and has not been submitted for a degree award at any other university.
Signed……………………………………………………………….Date……………………

Dr Iraya Anthony Mungai
MBChB (UON)
Post graduate student in Anesthesia, UON
Registration number H58/68603/2013

Supervisors’ declaration
This dissertation has been submitted for examination with our approval as University Supervisors.

Dr Chokwe T.M.
Senior Lecturer,
Department of Anaesthesia,
University of Nairobi
Signed……………………………………………………………….Date……………………

Dr Mwiti T. M.
Lecturer,
Department of Anaesthesia,
University of Nairobi
Signed……………………………………………………………….Date……………………

Dr Gatheru A.K.
Lecturer,
Department of Anaesthesia,
University of Nairobi
Signed……………………………………………………………….Date……………………
DEDICATION

To my beloved mother who gave me motivation to pursue a career in medicine and who herself is a breast cancer conqueror.

To my dear wife and children who have encouraged me daily and whom I love unconditionally.

And to my mentor Dr Muithya who gave me the passion to pursue anaesthesia.
ACKNOWLEDGEMENT

I sincerely thank the following:

The almighty God, for giving me strength and perseverance.

My three supervisors, Dr Chokwe, Dr Mwiti and Dr Gatheru for their continued support and encouragement since the start of this project.

Dr Philbert Murie and Mr. Martin Njenga for their dedication and passion towards this project.
# TABLE OF CONTENTS

DECLARATION ........................................................................................................... iii
DEDICATION .............................................................................................................. iv
ACKNOWLEDGEMENT ................................................................................................. v
TABLE OF CONTENTS ................................................................................................. vi
LIST OF TABLES AND FIGURES .............................................................................. viii
ABBREVIATIONS ......................................................................................................... ix
OPERATIONAL DEFINITIONS ...................................................................................... x
ABSTRACT ................................................................................................................... xi

## 1.0 CHAPTER ONE ................................................................................................. 1
  1.1 Introduction ........................................................................................................... 1
  1.2 Literature Review ................................................................................................. 1
  1.3 Surgical Treatment .............................................................................................. 2
  1.4 Post Mastectomy Pain Syndrome (PMPS) ........................................................ 2
  1.5 Pathophysiology ................................................................................................. 2
  1.6 Epidemiology of Post Mastectomy Pain Syndrome ........................................... 4
  1.7 Anaesthetic Interventions to Reduce PMPS ....................................................... 5
  1.8 Quality of Life for Patients with PMPS .............................................................. 6
  1.9 Assessment of Post Mastectomy Pain ............................................................... 6

## 2.0 CHAPTER TWO ................................................................................................. 8
  2.1 Study Justification ............................................................................................... 8
  2.2 Study question .................................................................................................... 8
  2.3 Objectives ......................................................................................................... 8
    2.3.1 Main Objective ............................................................................................. 8
    2.3.2 Specific objectives......................................................................................... 8

## 3.0 CHAPTER THREE: METHODOLOGY AND DATA MANAGEMENT ................. 9
  3.1 Study design ....................................................................................................... 9
  3.2 Study area description ....................................................................................... 9
  3.3 Study population ............................................................................................... 9
  3.4 Inclusion criteria ............................................................................................... 9
  3.5 Exclusion criteria ............................................................................................. 9
  3.6 Sampling technique ......................................................................................... 9
  3.7 Sample size determination .............................................................................. 9
  3.8 Data collection and management ................................................................... 10
  3.9 Data analysis ................................................................................................... 10
3.10 Study Limitations ........................................................................................................... 10
3.11 Ethical Consideration ...................................................................................................... 10
4.0 CHAPTER FOUR: RESULTS ........................................................................................... 11
5.0 CHAPTER FIVE DISCUSSION .......................................................................................... 18
5.1 Prevalence of Neuropathic Pain from Our Study; 61% and 48% at 1 and 3 Months
Respectively .......................................................................................................................... 18
5.2 Predictive factors associated with post mastectomy pain syndrome ......................... 18
5.3 Statistically Significant Association between Pain Control Post Operatively and Development of Neuropathic Pain at 1 and 3 Months ........................................................................................................................................ 19
6.0 CHAPTER SIX: CONCLUSIONS AND RECOMENDATIONS ........................................ 21
6.1 Conclusions ...................................................................................................................... 21
6.2 Recomendations ............................................................................................................... 21
REFERENCES ......................................................................................................................... 22
APPENDICES .......................................................................................................................... 24
Appendix I: Study Time Frame ............................................................................................ 24
Appendix II: Study Budget .................................................................................................... 25
Appendix III: Data Collection Questionnaires .................................................................. 26
Appendix IV: Consent Forms ................................................................................................. 34
Appendix V: Ethical Approval Form ...................................................................................... 44
Appendix VI: Antiplagiarism Certificate ............................................................................... 46
Appendix VI: KNH Statistics on Mastectomy ....................................................................... 47
LIST OF TABLES AND FIGURES

TABLES
Table 1: Demographical parameters of participants ................................................. 11
Table 2: Predictive variables for developing PMPS .................................................. 15
Table 3: Predictive variables for developing PMPS .................................................. 16
Table 4: Association between acute post operative pain and PMPS at 3 months .......... 17

FIGURES
Figure 1: Pain pathway .......................................................................................... 3
Figure 2: Age in years ........................................................................................... 12
Figure 3: Employment statistics ............................................................................ 12
Figure 4: Type of surgery ..................................................................................... 13
Figure 5: Pain intensity at 1 month post operatively ............................................. 13
Figure 6: Pain intensity at 1 month post operatively ............................................. 14
Figure 7: Neuropathic pain at 1 month ................................................................. 14
Figure 8: Neuropathic pain corresponding to PMPS at 3 months ......................... 15
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>American Society of Anesthesiologists</td>
</tr>
<tr>
<td>BCT</td>
<td>Breast conservative therapy</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>COX2</td>
<td>Cyclo-oxygenase 2</td>
</tr>
<tr>
<td>DRG</td>
<td>Dorsal root ganglia</td>
</tr>
<tr>
<td>EMLA</td>
<td>Eutectic mixture of local anesthetic</td>
</tr>
<tr>
<td>IASP</td>
<td>International Association for the Study of Pain</td>
</tr>
<tr>
<td>KNH</td>
<td>Kenyatta National Hospital</td>
</tr>
<tr>
<td>MRM</td>
<td>Modified radical mastectomy</td>
</tr>
<tr>
<td>NMDA</td>
<td>N-methyl-D-aspartate</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>Non steroidal anti inflammatory drugs</td>
</tr>
<tr>
<td>PAG</td>
<td>Periaqueductal gray area</td>
</tr>
<tr>
<td>PGE2</td>
<td>Prostaglandin E2</td>
</tr>
<tr>
<td>PMPS</td>
<td>Post mastectomy pain syndrome</td>
</tr>
<tr>
<td>PPMP</td>
<td>Persistent post mastectomy pain</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SLNB</td>
<td>Sentinel lymph node biopsy</td>
</tr>
<tr>
<td>SNRI</td>
<td>Serotonin and noradrenaline reuptake inhibitor</td>
</tr>
<tr>
<td>UON</td>
<td>University of Nairobi</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual analog scale</td>
</tr>
</tbody>
</table>
OPERATIONAL DEFINITIONS

A. **Chronic post surgical pain:** The International Association for the Study of Pain (IASP) has defined chronic pain as that persisting beyond the normal healing time of three months after a surgical procedure, having excluded other causes for pain such as infection or malignancy.

B. **Post mastectomy pain syndrome:** Continuous or intermittent pain occurring 2-3 months after breast surgery, having excluded other possible causes for the pain. The definition used for the purposes of this study was based on three criteria: timing of the pain, character of the pain, and pain location. The pain persists, either continuously or intermittently, beyond the normal healing time of three months. Typically neuropathic in character, described in terms of numbness, pins and needles, burning, tingling etc. The pain is located in the axilla, arm, shoulder, or chest wall on the side of surgery.

C. **Pain measurement tools:** The pain measurement tools chosen had been validated in previous studies:

   i. The Visual analogue scale (VAS) was used to quantify intensity of the pain, both acute post operative pain and chronic post mastectomy pain. For this study mild pain was a visual analogue scale of 1 to 2, moderate pain 3 to 5 and a score greater or equal to 6/10 severe pain.
   
   ii. The Douleur neuropathique four questionnaire (DN4) was used to assess neuropathic component of the post mastectomy pain syndrome.
   
   iii. The Brief pain Inventory was used to assess functional impairment. Functional impairment was analyzed by the mean scores of each of the 7 items on the Brief pain inventory

D. **Neuropathic pain:** initiated or caused by a primary lesion or dysfunction in the nervous system, which is characterized by hyperalgesia and alldynia. Often described as sensations of burning, lancinating, electric shock like, or stabbing. Usually felt in the region innervated by damaged nerves. In the DN4 form, scores above 4/10 was indicative of neuropathic component to the chronic pain.
ABSTRACT

**Background:** Post mastectomy pain syndrome (PMPS) is a common complication after mastectomy. This is pain persisting 2 to 3 months after mastectomy or any other type of breast surgery is performed. Post mastectomy pain remains a difficult to treat condition once it sets in, with significant consequences for the individual patient’s quality of life and cost of healthcare to society as a whole. A detailed description of PMPS would enable understanding of the magnitude of this problem and development of more effective pain management strategies at our institution.

**Objective:** The objectives of this study were to determine the prevalence of PMPS in patients undergoing mastectomy at KNH, as well as to determine any predictive factors for the development of PMPS. We also sort to establish any association between intensity of acute post surgical pain after mastectomy and development of post mastectomy pain syndrome.

**Materials and Methods:** This research was conducted as a prospective observational study after getting ethical approval from the Kenyatta National Hospital-University of Nairobi Ethics and research committee. 65 patients who underwent mastectomy at KNH between January 2016 and November 2016 were recruited using a consecutive sampling technique and followed up to 3 months post surgery using a telephone based interview.

A modified data collecting tool comprising the Visual analogue scale (VAS) and Douleur neuropathique four (DN4) was used to collect data via telephone at 1 and 3 months post mastectomy for each of the patients.

Collected data was analyzed using SPSS version 20. Descriptive statistics was used to determine the prevalence of PMPS. Regression analysis was undertaken to determine the influence of various independent variables on development of neuropathic pain. A paired sample t-test was run to determine association between intensity of acute post surgical pain after mastectomy and development of persistent post mastectomy pain.

**Results and discussion:** Results from 62 (95%) of patients was collected and analyzed. Majority of patients were between 61 and 80 years (50%), were married (48%) and underwent modified radical mastectomy (90%). Analgesic technique employed during mastectomy included an opioid with paracetamol with or without an NSAID (70%). Few patients received in addition a local anesthetic infiltration (13%). On first post operative day 50% reported moderate pain passively that increased to severe with active movement of ipsilateral upper limb. The prevalence of post mastectomy pain syndrome at 3 months was 48%. Neuropathic pain at 1 month was greater at 61%.

The results of the paired t-test carried out to find any association between acute pain post mastectomy and development of neuropathic pain showed the difference in means of pain intensity acutely post operatively (both passive and dynamic) and development of neuropathic pain at 1 and 3 months was statistically significant (p value 0.013).

**Conclusion:** Even with less invasive surgeries, PMPS remains a clinically significant problem. There is a significant association between control of acute post operative pain and development of neuropathic pain after mastectomy. Analgesic modalities utilized at our institution are devoid of adjuvant medication or regional analgesic techniques which might explain the poor acute post operative pain control and high PMPS prevalence.

**Key words:** Post mastectomy pain syndrome, prospective observational study, telephone based interview, regression and correlation analysis
1.0 CHAPTER ONE

1.1 Introduction
Persistent post surgical pain (PPP) is defined by the International Association for the Study of pain (IASP) as pain that develops after surgical intervention and lasts at least 2-3 months after healing has occurred, and other causes for the pain have been excluded.

Chronic pain is a common complication of surgery\(^1\) and overall, the incidence of chronic pain after major surgery has been estimated to lie between 20% and 50%.\(^2\) This incidence has been found to be higher after limb amputation (30-85%), mastectomy (11-57%), coronary bypass (30-50%) and inguinal hernia (5-63%) surgeries.\(^2\)

Various options have been advocated to prevent the development of chronic post surgical pain from occurring. Some of these include; public health measures to control modifiable diseases leading to surgical indication, early screening to diagnose diseases and medically treat or do less invasive surgical interventions, avoiding unnecessary surgery, minimally invasive surgical techniques, preventive multimodal analgesia that reduces intensity and severity of acute post surgical pain and that prevents its progression to chronic post surgical pain and identification and treatment of neuropathic symptoms post operatively using adjuvant medication, including antidepressants and anticonvulsants.

Persistent post surgical pain after mastectomy, also known as post mastectomy pain syndrome (PMPS) is a type of chronic post operative pain and persists 2-3 months after mastectomy or when other type of breast surgery is performed.

Post mastectomy pain is often neuropathic, but occasionally might occur due to hematoma or neuroma formation. It causes numbness, burning pain or dull ache. The pain is present in the chest area (site of surgery) as well as the axilla and ipsilateral arm. It is often worse on abduction of the arm and application to site of surgery.

Post mastectomy pain syndrome is a difficult to treat condition once it sets in, with significant consequences to patients’ quality of life and cost of healthcare.

1.2 Literature Review
Breast cancer is one of the leading cancers in Kenya, occurring in 34/100,000 women.\(^4\) With earlier diagnosis and treatment survival rates have began to improve, hence increasing the number of women for whom post treatment quality of life is important. In most cases, breast cancer is treated surgically, according to the clinical staging at the time of the diagnosis. Other modes of treatment include chemotherapy, radiotherapy and hormonal therapy.
1.3 Surgical Treatment
Surgery plays a crucial role in management of breast cancer with modified radical mastectomy being the most common type of surgery performed at KNH. This involves removal of the breast, skin, adipose tissue and ipsilateral axillary lymph nodes, with sparing of the pectoralis major and occasionally the pectoralis minor. Wide local excision/ Lumepectomy which is removal of the primary tumor with free margins together with a sentinel lymph node biopsy, is less invasive but is rarely performed.

Despite the efficiency of surgical treatment several complications have been reported, including lymphedema, wound sepsis and chronic postoperative pain.

Chronic pain secondary to the surgical procedure can be nociceptive – resulting from damage to muscles and ligaments; or neuropathic – resulting from damaged nerves or dysfunction of the nervous system. Neuropathic pain has been studied the most, since it is more common and corresponds to the post mastectomy pain syndrome (PMPS).

1.4 Post Mastectomy Pain Syndrome (PMPS)
Persistent pain after mastectomy was first reported by Wood in the 1970’s and is defined by the IASP as continuous or intermittent pain occurring 2-3 months after breast surgery, having excluded other possible causes for the pain.

The pain occurs at the anterior aspect of the thorax, axilla and/or ipsilateral upper limb. Jung et al distinguish four subtypes of neuropathic pain involved in PMPS;

1) Phantom breast pain – painful sensation on the breast removed.
2) Intercostobrachial neuralgia – pain and sensitivity changes in the distribution of the intercostobrachial nerve after mastectomy +/- axillary lymphadenectomy.
3) Pain secondary to development of neuroma, pain on the scar, thorax or arm triggered by percussion (Tinel’s sign).
4) Pain due to damage to other nerves.

1.5 Pathophysiology
The trauma and inflammation occurring from surgery activates nociceptors. Nociceptive stimuli are transduced into electrical impulses that are carried to the spinal cord via primary afferent A delta and C fibres. Primary afferent neurons synapse with secondary afferent neurons in the dorsal horn of the spinal cord and carry impulses to higher centers via the contralateral spinothalamic and spinoreticular pathways. There are then multiple projections to the cerebral cortex and other higher centers. Central processing of impulses leads to the experience of pain.
Inflammatory pain occurs because sensitizing, inflammatory mediators including cytokines, bradykinin and prostaglandins are released from injured and inflamed cells at the site of tissue damage. Nociceptors demonstrate reversible plasticity in response to inflammatory mediators. The activation threshold of nociceptors is lowered, resulting in enhanced pain sensitivity at the site of tissue injury, called peripheral sensitization.\(^9\)

NSAIDs inhibit production of PGE\(_2\) via locally induced COX2 enzymes and hence reduce peripheral sensitization and pain.\(^9\) This type of inflammatory pain, secondary to local excitability, usually subsides once the source of the mediators subsides, as tissue healing occurs.\(^10\) Heightened pain sensitivity can contribute to healing by helping to protect the damaged body part until healing has occurred.\(^9\)

The CNS also demonstrates plasticity in response to pain, and pain signaling within the spinal cord can be enhanced. With ongoing nociceptive input, the stimulus-response relationship is altered and an increase in excitability of neurons in the CNS may occur, known as central sensitization.\(^11\) Clinically this manifests as an increased response to normally painful stimuli (hyperalgesia), and pain secondary to normally non-painful tactile stimuli (allodynia).\(^11\)

Wind-up, long term potentiation and secondary hyperalgesia are all processes associated with central sensitization. Wind-up occurs with repeated activation of C fibres and is due to the activation of glutamate at the NMDA receptors. Under normal conditions, magnesium ion
blocks the NMDA receptor. With ongoing painful stimuli, the magnesium block is removed and the response of second-order neurons to painful stimuli is amplified. This explains why NMDA receptor antagonists, such as ketamine, are useful in attenuating or blocking wind-up.\textsuperscript{12}

The response of second-order neurons may outlast the initial stimulus and this is known as long term potentiation, contributing to hyperalgesia. A lowering of pain threshold outside the area of inflammation (secondary hyperalgesia) occurs because of increased activation of second-order neurons in the dorsal horn of the spinal cord.

Nerve damage plays a role in persistent post surgical pain. Following nerve injury, spontaneous ectopic discharge from injured nerves and nearby uninjured nerves leads to spontaneous pain.\textsuperscript{13} The increased nociceptive input to the dorsal horn leads to central sensitization.\textsuperscript{14} A loss of inhibitory interneurons in the dorsal horn results in disinhibition of pain pathways and facilitation of pain transmission.\textsuperscript{15}

The process of central sensitization is thought to be important for the development of persistent pain;\textsuperscript{16} hence, surgical techniques and pharmacological interventions to minimize central sensitization are of great interest.

1.6 Epidemiology of Post Mastectomy Pain Syndrome

Incidence and prevalence of persistent post mastectomy pain varies widely between studies, ranging between 25 to 60%.\textsuperscript{17,18} This wide variation across various studies is due in part to:
- Difference in duration of pain assessment from time of surgery
- Difference in pain assessment tool used
- Research methodology used
- Difference in clinical and socioeconomic character of various populations studied

To improve comparability, Jung et al suggested a consistent time frame definition of neuropathic pain after breast cancer surgery to be 3 months, the pain being continuous or intermittently present at the chest wall, axilla or ipsilateral arm.

In a prospective cohort study in the United States by Gildasio S. de Oliverra et al carried out between 2008 and 2011,\textsuperscript{35} 300 subjects were included with a median time from surgery to patient evaluation of 26 months. 110 patients (37\%) reported presence of chronic pain. 43\% reported pain to interfere with normal work, 33\% reported interference with general activity while 29\% reported interference with relationships. Axillary lymph node dissection was found to be associated with development of chronic pain. Younger age and high BMI was also shown to be associated with development of chronic pain. In that study intensity of acute post operative pain and post operative opioid consumption were not shown to influence development of PMPS.

In a cross-sectional observational epidemiological study on prevalence of chronic pain after surgery for breast cancer carried out in Denmark by OJ Vilholm et al between 2003 and 2004,\textsuperscript{34} a group of 258 breast cancer patients and 774 reference subjects were sent
questionnaires to assess prevalence of PMPS. Prevalence in the breast cancer group was 24% while in the reference group was 10%, with an odds ratio to developing PMPS after breast cancer surgery being 2.9 (95% CI 1.84-4.51). 3 significant risk factors were identified; having undergone breast surgery earlier, tumors located in the upper lateral breast quadrant and young age.

In a nationwide cross-sectional questionnaire study involving 3754 women aged 18-70yrs carried out in Denmark between January 2005 and December 2006 by Rune Gartner et al 36, prevalence of PMPS was 47%, with 13% severe pain, 39% moderate pain and 47% light pain. In this study factors found to be associated with chronic pain were young age, adjuvant radiotherapy and axillary lymph node dissection as compared to sentinel lymph node biopsy.

A descriptive cross-sectional study among 167 women in Egypt by Emad Hokkam et al from August 2010 to Jan 2012 37, showed a prevalence of 52%, most evident in young women and those with advanced tumor size. A significant decrease in prevalence was found among patients who underwent breast conservative treatment (BCT) and sentinel lymph node biopsy (SLNB) as opposed to modified radical mastectomy (MRM) with axillary dissection.

From these studies it is evident that PMPS constitutes a great challenge within post mastectomy patients, being more prevalent in younger women and those who undergo more invasive surgeries.

1.7 Anaesthetic Interventions to Reduce PMPS
Anesthetic interventions to reduce chronic pain after mastectomy have mainly focused on an anesthetic technique inclusive of a preventive, multimodal form of analgesia.

The practice of treating pain only after it has become well established is slowly being replaced by a preventive approach that aims to block the transmission of the primary afferent injury discharge, the inflammatory response, and ensuing ectopic activity. 20-23 This aims to reduce nociception and stress response during surgery, and block induction of central neural sensitization thus reduced intensity of acute post operative pain. By avoidance of afferent fibre recurrent discharge and thus peripheral and central sensitization, preventive analgesia also has the added advantage of preventing progression of acute post surgical pain to chronic post surgical pain.

Multimodal analgesia aims to use various analgesic classes of drugs and techniques using different routes of administration. This has been found to be more effective in studies that have focused on prevention of chronic post surgical pain following mastectomy;

Fassoulaki et al. 30 randomized 50 patients undergoing breast cancer surgery to one of two groups, in a double blinded study. Patients in the multimodal treatment group received gabapentin starting evening before surgery till day 8, transdermal EMLA cream beginning the day of surgery till day 3 and intraoperative ropivacaine irrigation of the brachial plexus and several intercostal spaces. Patients in the control group received placebo in place of the 3 active agents. At 3, but not 6 months after surgery, patients in the multimodal treatment
group had a significantly lower incidence of axillary pain (14 vs. 45%), arm pain (23 vs. 59%) and analgesic use (0 vs. 23%) compared with the placebo control group.

Iohom et al. 31 compared the efficacy of a comprehensive, preventive multimodal analgesic regimen to standard treatment in a randomized, non blinded trial of 29 women undergoing surgery for breast cancer (mastectomy or breast tumor resection with axillary node clearance). Patients in the treatment group (group S) received I.M morphine, diclofenac suppositories and dextropropoxyphene hydrochloride plus oral acetaminophen for 48h. Beginning 12h before surgery, patients in comprehensive group (group N) received I.V parecoxib followed by oral celecoxib till day 5 after surgery. In addition, before surgery, a paravertebral catheter was inserted and a continuous block established for up to 48h after surgery with bupivacaine. Finally patients in group N received oral acetaminophen for 48h. All patients received a general anesthetic for surgery. Pain intensity after movement was significantly lower in group S compared to group N across the 48h study period. A telephone interview 2-3 month later, conducted by a blinded interviewer, showed a significant lower incidence and intensity of chronic post operative breast surgery pain in group N (0%) than group S (85%).

A randomized double blind study by Dalia A. Nasr in Cairo, Egypt in 2013 on Efficacy of perioperative duloxetine on acute and chronic post mastectomy pain, 33 showed the SNRI significantly reduced post operative analgesic requirement, pain intensity and incidence of chronic pain at 3- and 6- month follow up in women undergoing breast surgery.

A double blinded placebo controlled trial by Abdullah S. Terkawi et al. 32 between 2009 and 2014 at the University of Virginia showed that perioperative I.V lidocaine administration was associated with decreased incidence of chronic post mastectomy pain.

1.8 Quality of Life for Patients with PMPS
Persistent post surgical pain is an increasingly recognized problem negatively impacting quality of life.24 Breast cancer is the most common form of female cancer, and with improved detection and treatment there has been an increase in number of survivors.

Among breast cancer patients, PMPS is rated the most troublesome symptom, 25 leading to disability and psychological distress, and is notably resistant to management. 26 Psychosocial factors such as anxiety, depression, sleep disturbance and catastrophizing have proven to be important contributors to the development of persistent pain post mastectomy. 2

1.9 Assessment of Post Mastectomy Pain
Adequate representation of pain requires more than one simple measure of pain intensity (unidirectional model). More commonly, researchers have found that two dimensions of pain self-report account for most of the variability in the way patients describe pain. Beecher (1959) called these dimensions “pain” and “reaction to pain”. A multidimensional model for
pain assessment would measure the “sensory” dimension of pain (intensity, or severity) and the “reactive” dimension of pain (interference with daily function).

The intensity of pain can be measured using the Visual analogue scale (VAS). The VAS has been used as a standard scale for rating pain. The reliability and validity of this scale among other pain scales has been accepted.\textsuperscript{19} This is a tool which incorporates a scale of 0 to 10, with 0 being no pain while 10 indicative of worst pain ever experienced. It also has a pictorial guide to assist in assessment of the pain.

The Douleur neuropathique 4 questionnaire (DN4) was validated in French and translated into English using appropriate procedures. It is comprised of 10 items (7 symptoms and 3 clinical examinations) and is easy to score with each item equally weighted with a score of 4 or more classifying the pain as neuropathic. The DN4 has a higher sensitivity (83\%) and specificity (90\%) than the other tools described.\textsuperscript{28}

The Brief Pain Inventory (BPI) has become one of the most widely used measurement tools for assessing clinical pain. The BPI allows patients to rate the severity of their pain and the degree to which their pain interferes with common dimensions of feeling and function. Initially developed to assess pain related to cancer, the BPI has been shown to be an appropriate measure for pain caused by a wide range of clinical conditions. In some ways, the BPI is a “legacy” instrument—a self-report measure that has, over time, become a standard for the assessment of pain and its impact.\textsuperscript{29}
2.0 CHAPTER TWO

2.1 Study Justification
Persistent post mastectomy pain is a common but under diagnosed and under recognized complication of surgery that has significant consequences for the individual patient’s quality of life, cost to healthcare and to society as a whole.

It is a difficult to treat problem heralding emotional and depressive components to its presentation. Hence identification of risk factors and instituting measures to mitigate against its occurrence would go a long way to improve quality of life for women post breast surgery and increase their satisfaction in surgery and anesthetic outcomes.

This study therefore aimed to outline this problem and identify gaps in healthcare at our institution which would go a long way to improve quality of care for our patients undergoing mastectomy and other surgical procedures.

Treatment of post mastectomy pain, like other forms of chronic pain is costly and a huge burden to society as a whole. Improved management of this condition would therefore reduce cost of healthcare for individuals and the society and improve quality of life.

There is currently no data available at our institution and the region on prevalence and severity of persistent post mastectomy pain. Data is especially lacking in a black African population with low socioeconomic status such as ours.

2.2 Study question
What is the prevalence and severity of post mastectomy pain syndrome at Kenyatta National hospital?

2.3 Objectives
2.3.1 Main Objective
To determine the prevalence, severity and predictive factors of developing Post mastectomy pain syndrome (PMPS) at Kenyatta National Hospital (KNH).

2.3.2 Specific objectives
1. To determine the prevalence of post mastectomy pain syndrome in patients undergoing mastectomy at KNH.
2. To determine the predictive factors for the development of PMPS after mastectomy at KNH.
3. To determine association between intensity of acute post surgical pain after mastectomy and development of post mastectomy pain syndrome.
3.0 CHAPTER THREE: METHODOLOGY AND DATA MANAGEMENT

3.1 Study design
This study was carried out as a prospective observational study between January 2016 and November 2016. It entailed following up patients undergoing mastectomy up to three months post mastectomy via a telephone based interview to assess prevalence and severity of post mastectomy pain syndrome.

3.2 Study area description
This study was carried out at the Kenyatta National Hospital, a level 6 referral hospital with a catchment population from Kenya and other east and central African countries. Patients were recruited from the surgical wards, followed up in theatre and evaluated on the first post operative day in the wards. A telephone based interview was conducted at 1 and 3 months after the mastectomy.

3.3 Study population
Patients were sampled from all patients undergoing mastectomy at Kenyatta National Hospital during the study period.

3.4 Inclusion criteria
All patients undergoing mastectomy during the study period who were in ASA I and II and consented to the study were recruited.

3.5 Exclusion criteria
Reasons for exclusion from the study included; patients who declined consent, patient with no access to telephone facility or with absolute language barrier and those with metastatically advanced breast cancer or in ASA III - VI.

3.6 Sampling technique
Being a finite population, sampling was conducted by consecutive sampling.

3.7 Sample size determination
Being a prospective observational study, sample size determination was done using Fischer’s formula with finite population correction:

\[ n = \frac{NZ^2p(1-p)}{d^2(N - 1) + Z^2p(1-p)} \]

\[ n = 59 + 10\% \text{ attrition} = 65 \]

Where:
\[ n = \text{sample size.} \]
Z=standard normal variant corresponding to the 95% confidence interval, and which is 1.96.

d = the required precision of the estimate (0.05).

p = the expected prevalence for post mastectomy pain syndrome, 0.3 $^{17-18}$

N = Finite population size, 88 $^{38}$, as per statistics on mastectomy from KNH registry.

3.8 Data collection and management
Two research assistants were recruited and trained on data collection and recording. All sampled patients scheduled for mastectomy were recruited and consent for a 3 month study taken from adult patients or their guardian if aged below 18 years. Demographic data was taken and pre-operative pain evaluation done night before surgery. Conduct of anesthesia, modes of analgesia and type of surgical procedure performed was recorded during the mastectomy. On first post-operative day assessment of intensity of acute post-operative pain (at rest and dynamic) using Visual analogue score (VAS) and type of post-operative analgesia used was recorded. A telephone based questionnaire administered at 1 and 3 months post-operatively in cooperating the VAS to assess pain intensity, DN4 to assess neuropathic component of the pain and the Brief pain Inventory for impairment of functionality was carried out by the principal investigator who was blinded from the earlier findings by the research assistants. Type of analgesia and adjuvant treatment (chemotherapy or radiotherapy) was also recorded.

3.9 Data analysis
Collected data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Descriptive statistics was used to determine the prevalence of PMPS. Regression analysis was undertaken to determine the influence of various independent variables on development of neuropathic pain. A paired sample t-test was run to determine association between intensity of acute post-surgical pain after mastectomy and development of persistent post mastectomy pain.

3.10 Study Limitations
The main limitations of the study were a small study population with some challenges encountered at telephone interview such as language miscommunication.

3.11 Ethical Consideration
Ethical approval was sought from the Kenyatta National Hospital-University of Nairobi Ethics and research committee before commencement of this study. Patients who consented to inclusion into this study were guaranteed of the utmost observance of confidentiality and were allowed to drop out at any time during the study period. Those who participated in the study did not receive any compensation and neither did they incur any cost. Patients who declined consent or dropped out of the study were not victimized and their care continued as intended. Those found to have significant post mastectomy pain were referred to the pain treatment clinic and appropriate options offered for management.
4.0 CHAPTER FOUR: RESULTS

Sixty five patients scheduled for mastectomy during the study period were recruited into the study. Two patients did not have their mastectomy done for surgical reasons. One patient died two weeks after discharge from hospital. Sixty two patients (95%) were recruited and followed up to three months after mastectomy and data collected was analyzed for prevalence of post mastectomy pain syndrome. All sixty two patients underwent balanced general anaesthesia with different types of analgesia as depicted below.

Table 1: Demographical parameters of participants

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 20</td>
<td>21 - 40</td>
</tr>
<tr>
<td>No.</td>
<td>1</td>
</tr>
<tr>
<td>%</td>
<td>1.6</td>
</tr>
<tr>
<td>Modal Class</td>
<td>61-80</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marital Status</th>
<th>Expenditure in USD per day</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alone</td>
<td>Married</td>
</tr>
<tr>
<td>No.</td>
<td>32</td>
<td>30</td>
</tr>
<tr>
<td>%</td>
<td>51.7</td>
<td>48.3</td>
</tr>
<tr>
<td>Modal class</td>
<td>Married</td>
<td>Greater than 1 but less than 2 USD</td>
</tr>
</tbody>
</table>

*Alone – Single and Widowed, DN4 - Douleur Neuropathique 4, RM - Radical Mastectomy, MRM – Modified Radical Mastectomy, L-Lumpectomy, SD-Standard deviation, USD - US dollars

As shown above majority of the patients were between 61 and 81 years (50%), were married (48%) and employed (74%). Most of the patients had a daily expenditure of more than two U.S dollars (51%).

Majority of the patients underwent modified radical mastectomy (90%), with 4.8% undergoing radical mastectomy and 3.2% lumpectomy.

Analgesic technique employed during mastectomy included a combination of an opioid with paracetamol plus or minus an NSAID in 43 cases (70%), while local wound infiltration was done in only 13 (20%) of the mastectomies.
Figure 2: Age in years

Figure 3: Employment statistics
Figure 4: Type of surgery

On first postoperative day, 25% had mild pain both passively and on active movement of the ipsilateral upper limb. 50% reported moderate passive pain that increased to severe on movement of the ipsilateral upper limb. 25% had severe pain passively and needed rescue analgesia. Postoperative analgesic regime consisted of either tramadol or pethidine for two days with either an NSAID or paracetamol of which patients were discharged on.
At one month majority of the patients reported moderate pain (58%), severe (26%) and mild (16%). None of the patients were on rescue analgesia. 20% of the patients were undergoing physiotherapy while 5% were using meditation for pain relief. Neuropathic pain symptomatology elicited using DN4 showed prevalence of 61% at one month.

At three months the pain intensity was moderate (53%), mild (32%) and severe (17%).
Prevalence of post mastectomy pain syndrome at 3 months was 48%.

![DN4 Score at three months post op](image)

Figure 8: Neuropathic pain corresponding to PMPS at 3 months

Table 2: Predictive variables for developing PMPS

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE</th>
<th>Wald’s statistic</th>
<th>Degrees of freedom</th>
<th>Significance</th>
<th>EXP(B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery Type 1</td>
<td>20.138</td>
<td>27741.192</td>
<td>0.000</td>
<td>1</td>
<td>0.999</td>
<td>557155677.4</td>
</tr>
<tr>
<td>Surgery type 2</td>
<td>20.266</td>
<td>27741.192</td>
<td>0.000</td>
<td>1</td>
<td>0.999</td>
<td>632855093.5</td>
</tr>
<tr>
<td>Body Mass Index(BMI)</td>
<td>0.298</td>
<td>0.277</td>
<td>1.156</td>
<td>1</td>
<td>0.282</td>
<td>1.347</td>
</tr>
<tr>
<td>Marital status Single</td>
<td>-0.610</td>
<td>0.854</td>
<td>0.514</td>
<td>1</td>
<td>0.474</td>
<td>0.543</td>
</tr>
<tr>
<td>Marital status Married</td>
<td>-0.839</td>
<td>0.740</td>
<td>1.288</td>
<td>1</td>
<td>0.256</td>
<td>0.432</td>
</tr>
<tr>
<td>Unemployment</td>
<td>-0.635</td>
<td>0.751</td>
<td>0.714</td>
<td>1</td>
<td>0.398</td>
<td>0.530</td>
</tr>
<tr>
<td>Age</td>
<td>0.341</td>
<td>0.462</td>
<td>0.545</td>
<td>1</td>
<td>0.460</td>
<td>1.407</td>
</tr>
<tr>
<td>Constant</td>
<td>-20.893</td>
<td>27741.192</td>
<td>0.000</td>
<td>1</td>
<td>0.999</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Surgery type1 - Radical mastectomy, Surgery type 2 – Modified radical mastectomy*
Table 3: Predictive variables for developing PMPS

<table>
<thead>
<tr>
<th>Row</th>
<th>Column</th>
<th>Controlled variable</th>
<th>Test</th>
<th>Value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>DN4 Score</td>
<td>Age</td>
<td>Partial correlation</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>BPI</td>
<td>Preoperative pain</td>
<td>-</td>
<td>Bivariate correlation</td>
<td>1</td>
<td>0.942</td>
</tr>
<tr>
<td>Surgery type</td>
<td>Pain Intensity</td>
<td>-</td>
<td>Chi square</td>
<td>7.365</td>
<td>0.599</td>
</tr>
<tr>
<td>Expenditure</td>
<td>BPI</td>
<td>-</td>
<td>Bivariate correlation</td>
<td>1</td>
<td>0.718</td>
</tr>
</tbody>
</table>

*BPI- Brief pain index, BMI- Body mass index

Using regression analysis, the odds of developing neuropathic pain or PMPS was strongly associated with the type of surgery, MRM vs. radical mastectomy, OR 1 (95% CI). This was not found to be statistically significant (p value 0.999) and could have been due to a small sample size, a possible limitation of the study.

Employed and married patients also had higher likelihood of getting PMPS (p values 0.256 and 0.398) and also not statistically significant.

Other associations found were young Age and high BMI, also not statistically significant (p values 0.460 and 0.282 respectively).

Following cross tabulation of the patients’ pain intensity (VAS) at 1 and 3 months against their daily incomes a Pearson Chi square test was carried out to ascertain the nature of association. The results showed there was a statistically significant association between pain intensity and income, with higher income being associated with higher pain intensity at 1 and 3 months (p-values 0.028 and 0.013).

Results of the paired t-test carried out to find any association between acute pain post mastectomy and development of neuropathic pain showed the difference in means of pain intensity acutely post operatively (both passive and dynamic) and neuropathic pain at 1 and 3 months was statistically significant (p value 0.013). This was most likely due to poor pain control.
Table 4: Association between acute post operative pain and PMPS at 3 months

<table>
<thead>
<tr>
<th>Paired VAS scores</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>SEM</th>
<th>95% CI of the difference</th>
<th>DF</th>
<th>t</th>
<th>Sig. (2 tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
<td>upper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. VASp Vs VAS1</td>
<td>-1.033</td>
<td>0.85</td>
<td>0.15</td>
<td>-1.351</td>
<td>-0.716</td>
<td>29</td>
<td>-6.656</td>
</tr>
<tr>
<td>2. VASa Vs VAS1</td>
<td>-0.533</td>
<td>1.106</td>
<td>0.20</td>
<td>-0.946</td>
<td>0.120</td>
<td>29</td>
<td>-2.641</td>
</tr>
</tbody>
</table>

VASp - Passive acute post-surgical pain, VAS a - Acute post-surgical pain when actively moving the arm, VAS1 - Persistent post-surgical pain at one month, SEM - Standard error in the mean, DF - Degrees of freedom, CI- Confidence interval
5.0 CHAPTER FIVE DISCUSSION

5.1 Prevalence of Neuropathic Pain from Our Study; 61% and 48% at 1 and 3 Months Respectively

In our study prevalence of neuropathic pain at one month was 61% and for post mastectomy pain syndrome it was 48%. This was in keeping with similar findings elsewhere where incidence and prevalence has been found to be between 25 to 60%\textsuperscript{17, 18}. This wide variation has been found to be because of various reasons;

Difference in duration of pain assessment from time of surgery has been shown to cause variability of results. As can be seen in our study level of neuropathic pain at one and two months was different between the same sample of patients. To improve comparability, Jung et al suggested a consistent time frame definition of post mastectomy pain syndrome to be neuropathic pain occurring 3 months after mastectomy. In our study we followed up patients up to 3 month using a telephone based questionnaire and this improved validity for our results.

Differences in type of pain assessment tools used also causes the wide range of results from various studies. In our study questionnaire we in cooperated the Douleur neuropathique 4 questionnaire (DN4), which has a high sensitivity (83%) and specificity (90%)\textsuperscript{28}.

Research methodology utilized also contributes to difference in results. Our study was a prospective study which enabled us to eliminate recall bias which would occur in retrospective studies. In randomized studies results are even more reliable since various arms are standardized except the independent variables being analyzed.

Differences in clinical and socioeconomic characters of various populations being studied also causes variability of results. In our study we tried to standardize the clinical status of our patients by picking ASA I and II patients without advanced metastatic disease. We also assessed for the daily expenditure of our patients to gauge their socioeconomic status, majority (51%) earning greater than 2USD. We also found out that patients with higher earnings were more likely to experience post mastectomy pain syndrome.

5.2 Predictive factors associated with post mastectomy pain syndrome

Various variables were analyzed to try and ascertain predictors for development of post mastectomy pain syndrome. Neuropathic pain at one month and PMPS at three months was strongly associated with type of surgery; Radical mastectomy vs. MRM using regression analysis OR 1 (95% CI). This means that patient who underwent more invasive surgery of radical mastectomy compared to modified radical mastectomy were more likely to develop post mastectomy pain syndrome. But this was not statistically significant (p value 0.999), possibly due to the small sample size. Similar findings have been reported in other studies.
In a descriptive cross sectional study of 137 patients in 2010 in Egypt by Emad Hokkam et al\textsuperscript{37}, found a PMPS prevalence of 52% with a significant decrease in prevalence in patients who had undergone less invasive surgery (Breast conservative therapy with Sentinel lymph node biopsy as opposed to Modified radical mastectomy with axillary dissection). In our study all our patients had axillary dissection.

Other associations found were young Age and high BMI, also not statistically significant (p values 0.460 and 0.282 respectively) also possibly due to small sample size. Other studies with larger sample sizes have demonstrated clearly this association.

A prospective observational cohort study in the US by Gildasio Oliviera et al\textsuperscript{35} which followed 300 patients up to six months after surgery found younger age OR 0.95 (95% CI) and axillary lymph node dissection as independent variables associated with development of chronic pain.

### 5.3 Statistically Significant Association between Pain Control Post Operatively and Development of Neuropathic Pain at 1 and 3 Months

Results of the paired t-test carried out to find any association between acute pain post mastectomy and development of neuropathic pain showed the difference in means of pain intensity acutely post operatively (both passive and dynamic) and development of neuropathic pain at 1 and 3 months was statistically significant (p value 0.013).

This was most likely due to poor pain control. Analgesics used during mastectomy mainly included an opioid regimen with paracetamol and an NSAID. Very few cases had local anaesthetic infiltration done. None of the cases had adjuvant medication (ketamine or clonidine) or regional techniques (pectoralis I and II block, paravertebral blocks or epidural blocks) utilized.

On first post operative day majority of the patients has moderate to severe pain. None of the patient were started on or discharged with adjuvant medication such as duloxetine, gabapentine or cabamazepine.

Various studies have shown the benefits of multimodal analgesic plan inclusive of regional technique and adjuvant medication in controlling acute post operative pain and subsequently reducing the magnitude of post mastectomy pain syndrome.

An RCT by Fassouki et al\textsuperscript{30} blindly randomized fifty women scheduled for breast cancer surgery into either of two groups; one receiving gabapentine two days preoperatively upto one week postoperatively, topical EMLA cream and local brachial plexus infiltration with ropivacaine and another receiving three placebos instead. The study demonstrated that multimodal analgesia reduces acute and chronic pain after breast surgery for cancer.
Dalia Nasir also carried out an RCT on fifty women scheduled for radical mastectomy and axillary dissection to assess the efficacy of perioperative duloxetine on acute and chronic post mastectomy pain. He randomized patients to one group taking duloxetine and another taking a placebo. Results showed that duloxetine significantly reduced post operative analgesic requirements, pain intensity and incidence of chronic pain at 3 and 6 months in women undergoing breast surgery.
6.0 CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions
1. Our study concluded that even with less invasive surgeries (90% modified radical mastectomy vs. 4.8% radical mastectomy in our study), post mastectomy pain syndrome remains a clinically significant problem, with prevalence similar to other studies performed elsewhere.

2. There is a significant association between control of acute post operative pain and development of neuropathic pain after mastectomy. We also noted that perioperative analgesic management of breast surgery was devoid of a multimodal technique inclusive of either adjuvant medication or a regional anaesthetic technique. This might have contributed to the poor post operative pain control and subsequent high magnitude of post mastectomy pain syndrome. Hence strategies of enhancing pain control perioperatively need to be improved at our facility.

3. More invasive surgery, young age, higher BMI, being married, employed and with higher income were found to be independent variables associated with development of post mastectomy pain syndrome. But none of these findings was statistically significant possibly due to a small sample size.

6.2 Recommendations
1. Optimization of perioperative pain control to reduce impact of post mastectomy pain syndrome, especially with in cooperation of local anaesthetic wound infiltration, regional anaesthetic techniques and perioperative adjuvant analgesia use.

2. Carrying out a larger multicentered, controlled study to better understand the magnitude of post mastectomy pain syndrome and its predictive factors.
REFERENCES


38. KNH statistics on mastectomy surgeries done in 2014 and between January – September 2015: Appendix VII.

### APPENDICES

Appendix I: Study Time Frame

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PROPOSAL DEVELOPMENT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETHICS APPROVAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DATA COLLECTION</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANALYSIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISSERTATION WRITING</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix II: Study Budget

<table>
<thead>
<tr>
<th>BUDGET ITEM</th>
<th>AMOUNT (Kshs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Fees for KNH-UON ERC</td>
<td>2000</td>
</tr>
<tr>
<td>Statistician consultation fee</td>
<td>30,000</td>
</tr>
<tr>
<td>Mobile phone</td>
<td>30,000</td>
</tr>
<tr>
<td>Stationery</td>
<td></td>
</tr>
<tr>
<td>(a) Printing</td>
<td>20,000</td>
</tr>
<tr>
<td>(b) Photocopying</td>
<td>5,000</td>
</tr>
<tr>
<td>(c) Binding</td>
<td>10,000</td>
</tr>
<tr>
<td>(d) Pens</td>
<td>1,000</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>36,000</strong></td>
</tr>
<tr>
<td>Research assistants</td>
<td>30,000</td>
</tr>
<tr>
<td>Contingency fund</td>
<td>30,000</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>158,000</strong></td>
</tr>
</tbody>
</table>

The budget was funded by the researcher’s employer, Ministry of State for Defence.
Appendix III: Data Collection Questionnaires

PREOPERATIVE ASSESSMENT
1. Age……………………………… Serial Number…………………
2. BMI…………
   a) Weight…………
   b) Height…………
3. Post menopausal
   o YES
   o NO
4. Marital status
   o Married
   o Single
   o Divorced
   o Widowed
5. Employment status
   o YES
   o NO
   o Self employed
6. How much do you use daily as expenses in Ksh……………..
7. ASA classification………..
8. Tumor staging………..
9. Pre-operative pain
   o Absent
   o Present. If so, Intensity……../10. Site……….. Duration………..
      Medication………..

![Pain Scale Image]
INTRA-OPERATIVE ASSESSMENT

1. Date of surgery………………… Serial Number……………………
2. Duration of surgery…………….HRS
3. Surgeon’s experience
   o Consultant
   o Registrar
4. Type of surgery
   o Radical mastectomy
   o MRM
   o Lumpectomy
5. Lymph node dissection done
   o Sentinel lymph node dissection
   o Total lymph node dissection/ Axillary dissection
6. Anesthetic plan
   o Balanced general anesthesia
   o Regional technique
7. Analgesic mode used
   o Opioid
   o Paracetamol
   o NSAIDS
   o Regional technique
   o Local wound infiltrations
   o Adjuvants
1. Visual analogue scale on intensity and severity of post operative pain:
   a. Passive……./10
   b. Dynamic with arm movement…./10

2. Location of pain……..

3. Character of pain……..

4. Analgesic regimen prescribed:

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>FREQUENCY</th>
<th>DURATION</th>
<th>ADVERSE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1) Maumivu yako kiasi gani kati ya moja na kumi?
   a) Ukiwa umepumzika…….../10
   b) Ukisongesha mkono......../10

![Pain Scale]

<table>
<thead>
<tr>
<th>No pain</th>
<th>Mild, annoying pain</th>
<th>Nagging, uncomfortable, troublesome pain</th>
<th>Distressing, miserable pain</th>
<th>Intense, dreadful, horrible pain</th>
<th>Worst possible, unbearable, excruting pain</th>
</tr>
</thead>
</table>

2) Uchungu upo pahali gani?............
3) Uchungu ni wa aina gani?............
4) Dawa ulizopewa ni zipi?

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>FREQUENCY</th>
<th>DURATION</th>
<th>ADVERSE EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Namba Tambulishi.............
ASSESSMENT AT 1 AND 3 MONTH TELEPHONE BASED INTERVIEW

A: English  
Serial Number……………………..

1. Visual analogue scale on intensity and severity of pain

![Visual Analogue Scale]

Score………/10

2. What is the character of your pain
   - Burning
   - Painful cold
   - Electric shock

3. Is the pain associated with
   - Tingling
   - Pins and needles
   - Numbness
   - Itching
   - Stabbing
   - Aching
   - Throbbing
   - Lancinating
   - Other………………

4. Is there numbness on surgical area associated with
   - Touch
   - Needle prick

5. Is the pain increased by contact with clothing?
   - Yes
   - No

6. What is the level of pain at its worst in last 24 hours………./10

7. What is the level of pain right now………./10

8. What percentage of pain relief have the pain medication provided………./100

9. In a scale 1-10 indicate to what level has your pain interfered with;
   a) General activity………./10
b) Normal house work………./10
   c) Relation with other people……../10

10. What type of rescue analgesia have you required ………………Number of times………

11. Have you undergone any of these adjuvant treatments?
   o Chemotherapy
   o Radiotherapy

12. What do you believe is the cause for your pain (catastrophizing)………………………………………………………………………………

13. Do you use any other method for pain relief? Y/N…… If yes, which one?
   o Physiotherapy
   o Acupuncture
   o Psychotherapy
   o Other……………………
B: Kiswahili

Namba Tambulishi………………

TATHMINI BAADA YA MWEZI MOJA NA TATU KWA NJIA YA SIMU

1) Maumivu yako kiasi gani kati ya moja na kumi?

![Rating Scale]

Kiasi………. /10

2) Uchungu ni wa aina gani?
   o Kuchoma
   o Uchungu baridi
   o Kama sitima

3) Uchungu unahusika na hali kama hizi?
   o Kuchoma chomwa
   o Kudungwa dungwa
   o Kuganda
   o Kuwashwa
   o Kuumwa
   o Nyingine………………

4) Kuna kuganda ulipopasuliwa kama
   o Umepashika
   o Ukidungwa na sindano

5) Uchungu waongezeka nguuo ikipashika?
   o Ndio
   o La

6) Maumivu yamekua kiasi gani kwa masaa 24 iliyopita?…………../10
7) Wastani kiasi ya uchungu ni kama upi?………../10
8) Ni asilimia ngapi ya kutuliza maumivu yanapata na dawa ulizopewa?........./ 100
9) Kipimo cha 1-10 eleza vile maumivu yanavyotatiza;
   a) Kazi za kawaida………………../10
   b) Kazi za ndani ya nyumba………./10
   c) Uhusiano na watu wengine……../10
10) Umetumia dawa zozote kwasababu uchungu umezidi? ……………..Mara ngapi?………..
11) Umepeata aina hii ya matibabu?
12) Unaamini ni nini kimesababisha maumivu yako? ……………………………

13) Unatumia njia zingine zozote kutuliza maumivu? Ndio/La……………Kama Ndio, ipi?
   o Mazoezi ya viungo
   o Acupuncture
   o Psychotherapy
   o Nyingine……………..
Appendix IV: Consent Forms
PREVALENCE OF POST MASTECTOMY PAIN SYNDROME (PMPS) AT KENYATTA NATIONAL HOSPITAL

This Informed Consent form is for surgical patients undergoing mastectomy at Kenyatta National Hospital general surgical wards and theatre. This consent will be administered to the patient. We are requesting these patients to participate in this research project whose title is “Prevalence of post mastectomy pain syndrome (PMPS) at Kenyatta National Hospital.

Principal investigator: Dr. Iraya Anthony Mungai
Institution: School of Medicine, Department of anesthesia- University of Nairobi
Supervisors: Dr. Chokwe, Dr. Mwiti, Dr. Gatheru

This informed consent has three parts:
1. Information sheet (to share information about the research with you)
2. Certificate of Consent (for signatures if you agree to take part)
3. Statement by the researcher
You will be given a copy of the full Informed Consent Form.
A. English
Part I: Information sheet

Background
My name is Dr Iraya Anthony, a post graduate student under Department of Anesthesia at the University of Nairobi, School of Medicine. I am carrying out a research to determine the prevalence of post mastectomy pain syndrome after Mastectomy at Kenyatta National Hospital. This will be a thesis contributing to part fulfilment of my degree of master of medicine (anesthesia) of the University of Nairobi.

I am going to provide you with information on the study and invite you to take part in it. Before you decide you can talk to anyone you feel comfortable with about the research. This consent form may contain words that you do not understand. Please ask me to stop as we go through the information and I will endeavour to clarify. If you feel the need to ask any questions later my contacts will be provided. You can ask me or any member of my team.

Purpose of the research
Pain after mastectomy is a common complication and may last up to many months after the surgery. This pain may also interfere with your ability to perform other duties when you return home.

This study aims to determine how common this complication occurs and also identify factors which might contribute to its occurrence. It will also try to establish the effect of chronic pain on your functionality when you go home.

Procedures
If you accept to take part in this research you will be required to fill an informed consent after being given information concerning the study as mentioned above. This will then be followed by filling questionnaires while in hospital by me or my two research assistants before surgery and on the morning after the operation to assess the level of pain. A telephone based interview at 1 and 3 months after the mastectomy will be conducted while at home. You shall be provided with a sample questionnaire to guide you at home on the questions to answer via telephone.

No names will be used on the questionnaires instead numbers will be assigned to the questionnaires. In addition on completion the questionnaires will be stored securely inside a lockable cabinet throughout the process of data entry and analysis. Nobody outside the research team will have access to them.

Voluntary participation
Your participation in this research is entirely voluntary. It is your choice; you may choose not to take part in this research. This choice will have no bearing on your treatment. You may change your mind later and stop participation even if you had agreed.
Duration
The administration of each questionnaire will not take more than twenty (20) minutes. The telephone based interviews will also take about the same duration and will be entirely at the cost of the researcher. You shall not bear any cost for the telephone interview.

Risk
Your involvement in this research will be through a personal and telephone based interview and you will not expose yourself to any risks if you consent to participate. Participation in this study is out of your own free will, you will not be denied medical care in case you refuse to participate in the study. You may stop participating at any time with no consequences whatsoever. All the information that you give us will be used for this research only.

Benefits
There will be no direct benefits to you for participating in this study. Your participation will help doctors identify how common chronic pain after mastectomy is in our hospital and also identify factors contributing to its occurrence and the impact it has on functionality of patients after mastectomy. If we identify you to have a high intensity of pain during your interview appropriate referral to pain treatment centres will be made.

Compensation
You will not be remunerated for taking part in this research.

Confidentiality
All the information which you provide regarding yourself and your condition will be kept confidential and no one but the researchers will see it. The information about you will be identified by a number and only the researchers can relate the number to yourself. The information will not be shared with anyone else unless authorized by the Kenyatta National Hospital/University of Nairobi – Ethics and Research Committee (KNH/UON-ERC). This proposal has been reviewed and approved by the KNH/UON-ERC which is a committee whose work is to make sure research participants are protected from harm.

Dissemination of results
The knowledge gotten from this research will be published so that interested persons may learn from the research. None of the findings will be attributed to you by name.

Whom to contact
In the event that you have any questions about the research that you would like answered you may ask through the contacts provided below:

- Secretary, KNH/UON-ERC
  P.O. Box 20723 KNH, Nairobi 00202
  Tel 726300-9
  Email: uonknh_erc@uonbi.ac.ke
• **Lead supervisor:**
  Dr Chowke T.M.
  Senior Lecture, Department of Anesthesia,
  University of Nairobi.
  Mobile phone 0722 528 237
  Email; tmchokwe@gmail.com

• **Principle researcher:**
  Dr. Iraya Anthony Mungai
  Department of Anesthesia, School of Medicine,
  University of Nairobi.
  P.O. Box 13857, Nairobi 00400
  Mobile phone 0723 443 947
  Email; anthonymungai13@gmail.com
Part 2: Consent Certificate

I……………………………………….from……………………………………
do agree to be part of the study the risks and benefits of which have been fully explained as by Dr Iraya A. Mungai. My participation is voluntary and will not be expecting any financial benefits.

Full name……………………………………
Sign …………………………………………
Date …………………………………………
Investigator’s signature ………………………

For any questions you can contact;

- **Principle researcher:**
  Dr. Iraya Anthony Mungai  
  Department of Anesthesia, School of Medicine, University of Nairobi.  
  P.O. Box 13857, Nairobi 00400  
  Mobile phone 0723 443 947  
  Email: anthonymungai13@gmail.com

- **Lead supervisor:**
  Dr Chowke T.M.  
  Senior Lecture, Department of Anesthesia, University of Nairobi.  
  Mobile phone 0722 528 237  
  Email: tmchokwe@gmail.com

- **Secretary, KNH/UON-ERC**  
  P.O. Box 20723 KNH, Nairobi 00202  
  Tel 726300-9  
  Email: uonknh_erc@uonbi.ac.ke
Part 3: Statement by the researcher
I have accurately read out the information sheet to the participant, and to the best of my ability made sure that the participant understands the following:

- Refusal to participate or withdrawal from the study will not in any way compromise the quality of care and treatment given to the patient.
- All information given will be treated with confidentiality.
- The results of this study might be published to enhance knowledge and to reduce complications for patients undergoing mastectomy.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the participant.
Name of researcher taking consent
Signature of researcher taking the consent
Date
B. Kiswahili
Sehemu ya kwanza: Maelezo ya Daktari mtafiti
Utangulizi

Madhumuni ya utafiti

Utaratibu

Ushiriki wa hiari

Muda kuja tathmini
Kila tathmini utachukua dakika ishirini hivi kuja. Mahojiano ya kutumia simu ya rununu yatajukua muda kama huo la kima yatakuwa kwa gharama ya mtafiti. Wewe hutachukua gharama yeyote kwa mahojiano ya simu.

Harari wa utafiti
Ushirika wako katika utafiti huu ni kwa binafsi na kupitia simu ya rununu na hii haitukuweka katika hatari kamwe. Ushirika wako ni kwa hiari yake, na usiposhiriki hatadhu matibabu yako. Maelezo yote utakayotupatia itatumika kwa utafiti huu pekeyake.

Faida ya Utafiti
Hakutakwa na faida ya moja kwa moja kwako kwa kushiriki kwa utafiti huu. Ushirika wako utasaidia madaktari kutumbua jinsi maumivu baada ya upasuaji wa mastectomy yanavyo adhiri
wanawake na pia kutambua mambo yanayochangia kwupo kwa uchungu huo. Ikiwa tutatambua uko na maumivu ya hali ya juu wakati wa mahojiano utapatiwa rufaa sahihi kwa vitu to vya matibabu.

**Fidia**
Hakutakuwepo na malipo kwa kuhusika kwako katika utafiti huu.

**Usiri**
Taarifa zote ambazo utatupa kukuhusu na hali yake ya afya itawekwa kwa siri na watafiti pekeyao wataweza kuionwa. Tathmini yako itatambulika kwa nambari tambulishi na watafiti pekee ndio watajua uhusiano wa nambari hiyo kwako. Taarifa zako hazitajulishwa kwa mtu yeyote ila kwa ibali ya Kenyatta National Hospital-University of Nairobi – Ethics and Research Committee (KNH-UoN-ERC). Utafiti huu uchambuliwa na kupewa idhini na KNH-UoN-ERC, kamati inayohakikisha wahusika wa utafiti hawadhulumiwi.

**Usambazaji wa matooke**
Maarifa tutakayo pata kutoka utafiti huu yatakapishwa wakuu wajifunze jinsi yakutatua maumivu haya. Matooke tutakayopata hayatahusishwa nawe.

**Wakuwasiliana naye**
Ikiwa uko na swali unaweza wasiliana na mmoja ya walioandikwa hapa chini;

- **Katibu, KNH/UON-ERC**
P.O. Box 20723 KNH, Nairobi 00202  
Tel 726300-9  
Email: uonknh_erc@uonbi.ac.ke

- **Msimamizi kiongozi;**
  Dr Chowke T.M.
  Mhadhiri mkuu, Department of Anesthesia,  
  University of Nairobi.
  Mobile phone 0722 528 237  
  Email: tmchokwe@gmail.com

- **Mtafiti mkuu:**
  Dr. Iraya Anthony Mungai  
  Department of Anesthesia, School of Medicine,  
  University of Nairobi.  
  P.O. Box 13857, Nairobi 00400  
  Mobile phone 0723 443 947  
  Email: anthonymungai13@gmail.com
Sehemu ya pili: Idhini ya mgonjwa
Namba Tambulishi………
Mimi ------------------------------------kutoka ---------------------------------------------nimekubali
kushiriki katika utafiti huu unaofanywa na Dkt. Iraya A. Mungai kutokana na hali ambayo
nimeelezwa na sio kwa malipo ama shurutisho lolote.

Jina la mshiriki............................................
Sahihi........................................................
Tarehe..........................................................
Sahihi ya Mtafiti..............................................

Kushotogumbamagazeti ya mshiriki
iwapo hawawezi sahihisha

Kwa maswali wasiliana na;

• **Mtafiti mkuu:**  
  Dr. Iraya Anthony Mungai  
  Department of Anesthesia, School of Medicine,  
  University of Nairobi.  
  P.O. Box 13857, Nairobi 00400  
  Mobile phone 0723 443 947  
  Email; anthonymungai13@gmail.com

• **Msimamizi kiongozi:**  
  Dr Chowke T.M.  
  Mhadhiri mkuu, Department of Anesthesia,  
  University of Nairobi.  
  Mobile phone 0722 528 237  
  Email; tmchokwe@gmail.com

• **Katibu, KNH/UON-ERC**  
  P.O. Box 20723 KNH, Nairobi 00202  
  Tel 726300-9  
  Email: uonknh_erc@uonbi.ac.ke
Sehemu ya tatu – Dhibitisho la mtafiti
Hii nikuidhinisha ya kwamba nimemueleza mshiriki kwenye utafiti kuhusu utafiti huu na pia nimempa nafasi ya kuuliza maswali. Nimemueleza yafuatayo;
- Kwamba kushiriki ni kwa hiari yake mwenyewe bila malipo.
- Kushiriki hakutasababisha madhara ama kuhatarisha maisha kamwe.
- Anaweza kujiondoa kutoka kwa utafiti huu wakati wowote bila kuhatarisha matibabu anayoyapata katika hospital kuu ya Kenyatta.
- Habari ambazo atapeana hazita tangazwa hadharani bila ruhusa kutoka kwake (mshiriki) na pia kutoka kwa mdhamini mkuu wa utafiti wa hospital kuu ya Kenyatta na chuo kikuu cha matibabu.

Jina la Mtafiti ………………………………………
Sahihi………………………………………………
Tarehe………………………………………………
Appendix V: Ethical Approval Form

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

4th April, 2016

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

Ref: KNH-ERC/A/116

Dr. Iraya A. Mungai
Reg. No. H58/68603/2013
Dept. of Anaesthesia
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Iraya,

Revised Research Proposal: Prevalence of Post Mastectomy Pain Syndrome (PMPS) at Kenyatta National Hospital (P18/01/2016)

This is to inform you that the KNH-UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and approved your above proposal. The approval period is from 4th April 2016 – 4th April 2017.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal).
f) Clearance for export of biological specimens must be obtained from KNH-UoN ERC for each batch of shipment.
g) Submission of an executive summary report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH-UoN ERC website http://www.erc.uonbi.ac.ke
Yours sincerely,

PROF. M.L. CHINDIA
SECRETARY, KNH- UoN ERC

c.c. The Principal, College of Health Sciences, UoN
     The Deputy Director, CS, KNH
     The Chair, KNH- UoN ERC
     The Dean, School of Medicine, UoN
     The Chair, Dept. Anaesthesia, UoN
     Supervisors: Dr. Chckwe T. M, Dr. Mwiti T.M, Dr. Gatheru A.K
Appendix VI: Antiplagiarism Certificate

Turnitin Originality Report

PREVALENCE OF POST MASTECTOMY PAIN SYNDROME (PMPS) AT KENYATTA NATIONAL HOSPITAL by Iraya Mungai
From Anaesthesia (Medicine)

- Processed on 16-Jul-2017 13:34 EAT
- ID: 831091381
- Word Count: 8975

Similarity Index
14%

Similarity by Source

Internet Sources: 9%
Publications: 8%
Student Papers: 7%

souces:

1. 1% match (Internet from 07-May-2016)

2. 1% match (Internet from 11-Jun-2014)

3. 1% match (Internet from 21-Mar-2015)

4. 1% match (Internet from 25-Feb-2014)
   http://di.womeniq.net/b/bda4b416-56f9-4179-a75a-e102e933c0b1.pdf

5. 1% match (Internet from 04-May-2016)

6. 1% match (publications)

7. 1% match (student papers from 25-Apr-2014)
   Submitted to Ashesi University on 2014-04-25

8. < 1% match (Internet from 17-May-2016)
Appendix VI: KNH Statistics on Mastectomy

### Number of Mastectomy Surgeries done - Jan - September 2015

<table>
<thead>
<tr>
<th>Operations on the breast</th>
<th>Alive</th>
<th>Dead</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-861 Complete mastectomy</td>
<td>14</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>5-862 Extended simple mastectomy</td>
<td>37</td>
<td>0</td>
<td>37</td>
</tr>
<tr>
<td>5-863 Radical mastectomy</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5-864 Extended radical mastectomy</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5-869 Other excision of breast</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>63</td>
<td>0</td>
<td>63</td>
</tr>
</tbody>
</table>

### Number of Mastectomy Surgeries done - Year 2014

<table>
<thead>
<tr>
<th>Operations on the breast</th>
<th>Alive</th>
<th>Dead</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-861 Complete mastectomy</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>5-862 Extended simple mastectomy</td>
<td>58</td>
<td>0</td>
<td>58</td>
</tr>
<tr>
<td>5-863 Radical mastectomy</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>5-864 Extended radical mastectomy</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>5-869 Other excision of breast</td>
<td>17</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>88</td>
<td>0</td>
<td>88</td>
</tr>
</tbody>
</table>

Source: Health Information Department

02/12/2015

Assistant Director of Health
Kenyatta National Hospital

2 DEC 2015

P.O. Box 20723 - 00202
NAIROBI