

Sudan University of Science and Technology

College of Graduate Studies

***Measurement of Radioactivity in Breast Milk
Following Administration of TC^{99m} to the
Thyroid Gland***

قياس النشاط الاشعاعي في لبن الام بعد حقن عنصر التكنيشيوم-99م
لفحص الغدة الدرقية

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الآيه

قال تعالى

بسم الله الرحمن الرحيم

اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ (1) خَلَقَ الْإِنْسَانَ مِنْ عَلَقٍ (2) اقْرَأْ وَرَبُّكَ الْأَكْرَمُ (3)
الَّذِي عَلَّمَ بِالْقَلَمِ (4) عَلَّمَ الْإِنْسَانَ مَا لَمْ يَعْلَمْ (5)

سورة العلق

Dedication

I dedicate this research to

My mother

My father

My husband

My little son and

My teachers

Acknowledgement

First, great thanks to Allah, the Almighty who made all things possible and gave me the power to accomplish this research. I would like to present a great gratitude to my supervisor Dr.Salah Ali Fadlalla for his guidance and support. Also I like to extend my great appreciation to the staff of Sudan University of Science and Technology, particularly the college of medical radiologic science

The successful completion of this study would not be accomplished without the assistance and cooperation of the staff of Al Nelein Diagnostic center, so I would like to thank them for their cooperation and assistance.

Abstract

This study was conducted at Al Nelain diagnostic center during the period from November 2016 to April 2017. The main objective of the study was to measure and calculate the amount of radioactivity excreted in breast milk after administration of 185 MBq of $^{99m}\text{TcO}_4$ to thyroid scan patients as well as estimation of the dose received by the baby from the ingestion of the milk. The study came out with many results including the average activity per 140ml of milk for 15 patients at 12 hours which was 0.65 MBq and it decreased monoexponentially to reach 0.07 MBq after 24 hours with an effective half life of 4.8 hours. Using these data, the effective dose equivalent to the babies for the administered activity were found between 0.183 And 0.498 mSv. The results, as well, showed that there was no need for breast feeding interruption more than 12 hours to achieve less than 1 mSv effective dose equivalent to the baby as this rate was compatible with the ICRP standard (less than 1 mSv per year). In case of greater activities the percentage of activity excreted can be applied to calculate the excreted activity and estimation of the interruption of breast feeding period. The results showed an inverse relationship between the thyroid uptake and the excreted activity was established.

الخلاصة

أجريت هذه الدراسة في مركز النيلين التشخيصي في الفترة ما بين نوفمبر 2016 إلى ابريل 2017 بهدف قياس النشاط الإشعاعي في حليب الأم بعد حقن 185 ميغابيكيرل من عنصر التكنيشيوم لفحص الغدة الدرقية وقياس جرعة الإشعاع التي يتلقاها الرضيع من حليب الأم. توصلت الدراسة إلى عدد من النتائج أهمها أن متوسط النشاط الإشعاعي لعدد 15 مريضا لكل 140 مليلتر من الحليب هو 0.65 بعد مرور 12 ساعة من حقن التكنيشيوم ثم تناقصت لتصل الى 0.07 بعد مرور 24 ساعة حيث كان عمر النصف الفعال 4.8 ساعة. باستخدام بيانات الدراسة تم حساب الجرعة المكافئة للطفل بعد معاودة الرضاعة ووجد انها تتراوح ما بين 0.183 و 0.498 مليسيفرت. كما أشارت النتائج الى انه لاضرورة لوقف الرضاعة لمدة أكثر من 12 ساعة من توقيت الحقن للحفاظ على جرعة مكافئة اقل من 1 مليسيفرت وهي الجرعة المكافئة السنوية المسموح بها بحسب معايير و قوانين اللجنة الدولية للوقاية الإشعاعية. عند استخدام كميات اكبر من النشاط الاشعاعي يمكن استخدام ثابت نسبة النشاط الاشعاعي لتحديد كمية النشاط الاشعاعي وتبعاً لذلك مدة إيقاف الرضاعة عن الطفل. كما اشارت الدراسة الى وجود علاقة عكسية بين نشاط وامتصاص الغدة الدرقية وكمية النشاط الاشعاعي في حليب الأم. تم وضع بعض التوصيات فيما يتعلق بهذه الدراسة التي يمكن الاستفادة منها في تقليل الجرعة الاشعاعية المكافئة للطفل وتقليل زمن التوقف عن الرضاعة.

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List of abbreviations

$^{99m}\text{TcO}_4$	Technitium Per technetate
CT	Computed Tomography
ED	Effective Dose
EDE	Effective Dose Equivalent
ICRP	International Commission on Radiological Protection
ID	Injected dose
Kev	Kiloelectron volt
MBq	Megabecquerel
MRI	Magnetic Resonance Imaging
mSv	Millisievert
SPSS	Statistical Package for Social Science
$T^{1/2}$	Half life
TDLU	terminal ductal lobular units
TSH	Thyroid Stimulating Hormones
US	Ultra Sound

CHAPTER ONE

INTRODUCTION

Chapter One

Introduction

1.1 Introduction

The radioisotope Tc^{99m} is commonly used for nuclear medicine departments for the majority of examinations. Since these examinations may be administered to a breast feeding mothers, a spot light should be focused on such patients since Administration of Tc^{99m} pertechnetate into a breastfeeding mother can carry a significant risk to the baby after ingestion of their milk. Such hazard can be reduced or avoided by interrupting breast feeding for a period of time. Since the milk is important and constitutes a life necessity to the infant, we cannot delay it longer than it should be, and at the same time cannot introduce a radioactivity to an infant's body without a necessity. For the previous reasons there is an importance of precise measurements to estimate the amount of activity following the administration of Tc^{99m} to lactating mothers. This will be estimated upon specific calculations and measurements of the remaining activity in breast milk. The targeted sample will be thyroid scan patients since they are injected with Tc^{99m} pertechnetate which constitute the majority of examinations in the area under study.

1.2 problem of the study

Despite the importance of measuring the radioactivity in mother's milk after administration of Tc^{99m} such research has never been done in the area of the study. One of the researcher limitations is the absence of comparable studies under the area of study.

1.3 Objectives

1.3.1 General objective

To measure the Tc^{99m} radioactivity excreted in breast milk after the injection of $^{99m}TcO_4$ to thyroid scan patients.

1.3.2 Specific objectives

- To calculate the exact time needed for the radioactivity to be cleared out of the mother's milk specifically in Alnelain diagnostic center.
- To estimate the lowest time to resume breastfeeding.
- To estimate the radiation dose to the baby from the mother's milk.

1.4 Importance of the study

The study has never been done before pertaining to the estimation of the radiation hazard to the baby by ingestion breast milk or by direct contact to the mother to the best of the researcher knowledge. Since the babies are very sensitive to radiation doses, the exact time to resume breast feeding after administration of Tc^{99m} is needed. In addition, not every mother is able to express milk effectively. After a prolonged interruption it may be very difficult to resume feeding. It is therefore vital to disturb the breast feeding routine as little as possible.

CHAPTER TWO
LITERATURE REVIEW

Chapter Two

Literature Review

2.1 Theoretical background

2.1.1 Preamble

Since the 1990s the advantages of breastfeeding have been emphasized and the number of women who nurse their infant has increased significantly. Although women in this population are generally healthy and relatively rarely need radionuclide imaging or radionuclide therapies, the issue of radiation protection of breastfed children arises because of their higher radiosensitivity. Generally, administration of radiopharmaceuticals to mothers who are breastfeeding is avoided because the activity is secreted into the breast milk, potentially exposing the infant to unwanted radiation. This is of special concern since infants are comparatively highly sensitive to radiation, have a long life expectancy, and do not derive any direct benefit from the clinical examination. When it is vital for the mother to have an examination performed it is, in some situations, necessary to temporarily interrupt breastfeeding. This interruption may cause feeding problems and beyond a certain length of time it may be difficult for the mother to maintain her milk supply and be able to begin breastfeeding again. Breastfeeding is very important for both the infant and the mother. Unfortunately, breastfeeding is too often terminated unnecessarily. On the contrary, in those situations when a necessary termination of breastfeeding is ignored, serious harm to the infant may appear, since locally high absorbed doses (e.g. to the thyroid) may be of deterministic levels. (Leide-Svegborn et.al 2015).

With this background and the fact that examinations in patients who are breastfeeding are not routine and rarely performed, it is important to have

access to proper, clear recommendations on the duration of a feasible interruption of breastfeeding. Such recommendations should be based on accurate biokinetic and dosimetric data. Systematically collected data on the excretion of radionuclides into breast milk are rare. Data are often published in the form of case reports. There are also some reviews based mainly on compilations of data published previously.

The European Union recommendations from 1998 suggest interrupting breastfeeding after administration of several radiopharmaceuticals and measuring the activity in the expressed breast milk before resuming breastfeeding. This might be preferable, but it is not always practical since a thorough dose estimate requires measuring the activity in numerous breast milk samples at various times after administration of the radiopharmaceuticals. This means that the patient has to return to the hospital or that a healthcare worker has to collect the breast milk several times after the examination. This is neither practically nor economically feasible, particularly when the patient lives far away from the hospital. In 2008 the International Commission on Radiological Protection (ICRP) published more extensive recommendations including 47 different radiopharmaceuticals. Many of the studies contributing to the recommendations were based on a small number of patients and measurements. It is important to continue to collect biokinetic data and to continue dosimetric analysis in the infant of the nuclear medicine patient who is breastfeeding. This study considerably extends our previously published database, and we improved the dosimetry using specific absorbed fractions (SAF values) derived for newborn infants and radiopharmaceutical-specific biodistribution. The absorbed dose to organs and tissues and the effective dose to the newborn infants were estimated using the whole material. (Leide-Svegborn et.al 2015)

2.1.2 Female breast anatomy

The rudimentary breasts are identical in both sexes at birth and for few years afterwards. The breast or the mammary glands are modified skin glands which imbedded in the fatty tissue. The mammary gland in fact is composed of 15 -25 individual and independent glands having separate and lactiferous ducts. The adult female breasts are paired subcutaneous organs on the anterior thorax lying completely within the superficial and deep layers of superficial pectoral fascia. Adult mature female breast is mature breast and of different shapes and sizes of different women. The size and shapes depends on genetic, racial and dietary factors along with age and menopausal status of the women. The size of the base of the breast is fairly constant in almost all women (Neville, March 2001).

The breast lies in front of 2 to 6 rib in the mid clavicular line. The breast lies over the pectoralis major muscle and extends to serratus anterior and external oblique muscle of the abdomen. Axillary tail is lateral extension of breast tissue into axilla. Both breasts consist of nipple, areola and breast tissue. The left breast is generally larger than the right, and the weight varies in different individuals and at different times. For example, a single breast in a non pregnant woman may weigh 200 g. By the end of pregnancy it may weigh 400 to 600g and during lactation may increase to 600-800 g (Neville, March 2001).

The mesenchymal tissue present around growing ductal tissue changes into dense connective tissue dividing the whole breast into 15-25 lobes. There are about 15-25 main mammary ducts in each breast. These open on the summit of the nipple through separate openings. Each duct has dilated part called ampulla just before its opening on to the nipple. Each main duct drains a lobe of the breast. Each lobe is further divided into lobules and acini. Each lobe is irregularly lobulated as shown in figure (2.1) (Neville, March 2001).

Each lobule has a collection of 10-100 acini or terminal ductal lobular units. It consists of extra and intra lobular terminal ductule, alveoli, terminal ductal lobular units [TDLU]). Some secretions are also present in these ductules. Non lactating breast consists of more fibrous tissue and less glandular tissue (almost only ducts) (Neville, March 2001).

The growth of mammary tissue beneath the areola occurs at the age of 10 years. It is called breast bud. True nipple develops at about 12 years of age followed by 2-3 years growth of breast tissue. Then there is areolar recession and the breast takes a classical shape.

The size of breast in females enlarges at puberty by the action of estrogens. The areola becomes recognizable as the nipple has myoepithelial cells (erectile tissue) in its dermis which makes the nipple erect on stimulation. Areola has sweat glands, and subaceous glands present in its dermis. The sebaceous glands enlarge during pregnancy and are called tubercles of Montgomery (Neville, March 2001).

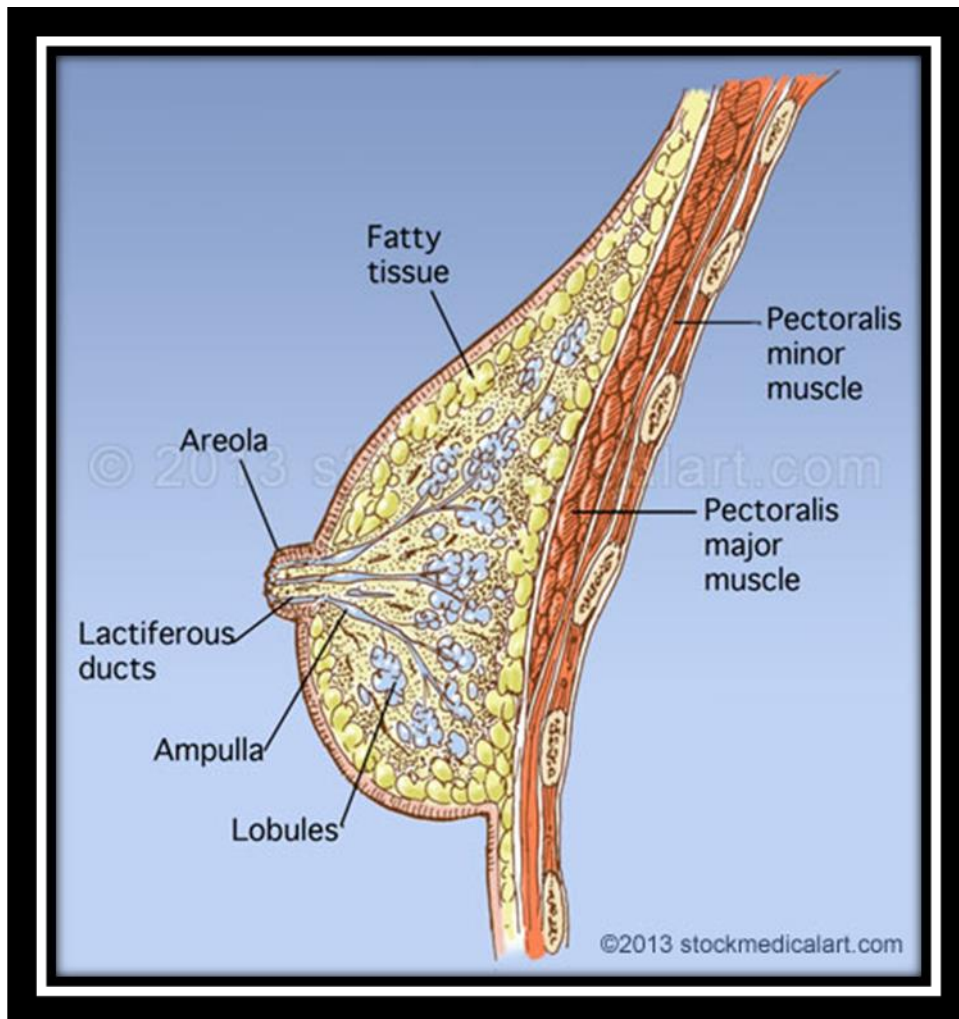


Figure (2.1) Anatomy of the breast

Fascia is present beneath the breast which is the continuation of the fascia of Scarpa (sub mammary fascia). Submammary space is present between this fascia and fascia over pectoralis major muscle. The fascia is continuous above with superficial cervical fascia and below with Camper's fascia. Lymphatic plexus is present in the sub mammary space. Young breast has fibrous tissue strands which connect deep fascia with deeper layers of the dermis. These are called ligaments of Astley Cooper. These keep the breast protuberant and well shaped. These strands get atrophic in elderly women and breasts become pendulous (Neville, March 2001).

During pregnancy there is an increase in size and density of the breasts. Glandular tissue fills all of the central portion of the breast. It happens due to stimulatory effects of large quantities of placental estrogens. These lead to proliferation and branching of ductal system. Additional quantities of growth hormone and prolactin lead to growth and branching of ductal system. Glucocorticoids and insulin also have some role in this process of proliferation. Stromal tissue of breast increases and the deposition of fat also increases simultaneously (Neville, March 2001).

2.1.3 Breast physiology

2.1.3.1 Development of the Breasts

The breasts begin to develop at puberty. This development is stimulated by the estrogens of the monthly female sexual cycle, estrogens stimulate growth of the breasts' mammary glands plus the deposition of fat to give the breasts mass. In addition, far greater growth occurs during the high- estrogen state of pregnancy, and only then does the glandular tissue become completely developed for the production of milk (Neville, March 2001).

2.1.3.2 Growth of the Ductal System and Role of the Estrogens

All through pregnancy, the large quantities of estrogens secreted by the placenta cause the ductal system of the breasts to grow and branch. Simultaneously, the stroma of the breasts increases in quantity, and large quantities of fat are laid down in the stroma. Also important for growth of the ductal system are at least four other hormones: growth hormone, prolactin, the adrenal glucocorticoids, and insulin. Each of these is known to play at least some role in protein metabolism, which presumably explains their function in the development of the breasts.

2.1.3.3 Pregnancy and Lactation

- Development of the Lobule-Alveolar System—Role of Progesterone

Final development of the breasts into milk-secreting organs also requires progesterone. Once the ductal system has developed, progesterone—acting synergistically with estrogen, as well as with the other hormones just mentioned—causes additional growth of the breast lobules, with budding of alveoli and development of secretory characteristics in the cells of the alveoli. These changes are analogous to the secretory effects of progesterone on the endometrium of the uterus during the latter half of the female menstrual cycle.

- Initiation of Lactation and Function of Prolactin

Although estrogen and progesterone are essential for the physical development of the breasts during pregnancy, a specific effect of both these hormones is to inhibit the actual secretion of milk. Conversely, the hormone prolactin has exactly the opposite effect on milk secretion—promoting it. This hormone is secreted by the mother's anterior pituitary gland, and its concentration in her blood rises steadily from the fifth week of pregnancy until birth of the baby, at which time it has risen to 10 to 20 times the normal nonpregnant level (Neville, March 2001).

Immediately after the baby is born, the sudden loss of both estrogen and progesterone secretion from the placenta allows the lactogenic effect of prolactin from the mother's pituitary gland to assume its natural milk-promoting role, and over the next 1 to 7 days, the breasts begin to secrete copious quantities of milk instead of colostrum. This secretion of milk requires an adequate background secretion of most of the mother's other hormones as well, but most important are growth hormone, cortisol, parathyroid hormone, and insulin. These hormones are necessary to provide the amino acids, fatty acids, glucose, and calcium required for milk formation. After birth of the baby,

the basal level of prolactin secretion returns to the nonpregnant level over the next few weeks. However, each time the mother nurses her baby, nervous signals from the nipples to the hypothalamus cause a 10- to 20-fold surge in prolactin secretion that lasts for about 1 hour. This prolactin acts on the mother's breasts to keep the mammary glands secreting milk into the alveoli for the subsequent nursing periods. If this prolactin surge is absent or blocked as a result of hypothalamic or pituitary damage or if nursing does not continue, the breasts lose their ability to produce milk within 1 week or so. However, milk production can continue for several years if the child continues to suckle, although the rate of milk formation normally decreases considerably after 7 to 9 months (Neville, March 2001).

Ejection (or "Let-Down") Process in Milk Secretion and Function of Oxytocin

Milk is secreted continuously into the alveoli of the breasts, but milk does not flow easily from the alveoli into the ductal system and, therefore, does not continually leak from the breast nipples. Instead, the milk must be ejected from the alveoli into the ducts before the baby can obtain it. This is caused by a combined neurogenic and hormonal reflex that involves the posterior pituitary hormone oxytocin, as follows. When the baby suckles, it receives virtually no milk for the first half minute or so. Sensory impulses must first be transmitted through somatic nerves from the nipples to the mother's spinal cord and then to her hypothalamus, where they cause nerve signals that promote oxytocin secretion at the same time that they cause prolactin secretion. The oxytocin is carried in the blood to the breasts, where it causes myoepithelial cells (which surround the outer walls of the alveoli) to contract, thereby expressing the milk from the alveoli into the ducts at a pressure of +10 to 20 mm Hg. Then the baby's suckling becomes effective in removing the milk. Thus, within 30 seconds to 1 minute after a baby begins to suckle, milk begins to flow. This process is called milk ejection or milk let-down. Suckling on one breast causes

milk flow not only in that breast but also in the opposite breast. It is especially interesting that fondling of the baby by the mother or hearing the baby crying often gives enough of an emotional signal to the hypothalamus to cause milk ejection (Neville, March 2001).

2.1.4 Milk composition and the metabolic drain on the mother caused by lactation

At the height of lactation in the human mother, 1.5 liters of milk may be formed each day (and even more if the mother has twins). With this degree of lactation, great quantities of metabolic substrates are drained from the mother. For instance, about 50 grams of fat enter the milk each day, and about 100 grams of lactose, which must be derived by conversion from the mother's glucose. Also, 2 to 3 grams of calcium phosphate may be lost each day unless the mother is drinking large quantities of milk and has an adequate intake of vitamin D, the output of calcium and phosphate by the lactating mother will often be much greater than the intake of these substances. To supply the needed calcium and phosphate, the parathyroid glands enlarge greatly, and the bones become progressively decalcified. The mother's bone decalcification is usually not a big problem during pregnancy, but it can become more important during lactation (Neville, March 2001).

If we take a deeper look at There are 4 processes of excretion from the alveolar cells into the lumen. 1. Proteins, carbohydrate, calcium, phosphate, and citrate are packaged into secretory vesicles and secreted by exocytosis. The proteins are made predominantly in the breast from amino acids derived from the blood or synthesized in the breast tissue and include casein, a-lactalbumin, and b-lactalbumin. The plasma derived proteins occur predominantly in the colostrum in the first few days of lactation. The predominant carbohydrate is lactose, which is synthesized in association with the Golgi apparatus in the cell, from

circulating glucose. The concentration of lactose in milk is constant, and this appears to be the limiting factor in the volume of milk produced. Calcium, phosphate, and citrate are transported into the Golgi vesicles from the cytoplasm. Water is drawn into the Golgi by osmosis. 2. Lipids and triglyceride are formed within the cell and coalesce to form large droplets that gradually make their way to the top of the alveolar cell, where they are enveloped in apical plasma membrane. The milk fat globule then separates from the cell. Milk fat composition is altered by diet. 3. Monovalent ions and water penetrate the apical membrane freely. Water and sodium and potassium ions move across the membrane in response to the osmotic gradient set up by the lactose, and the electrolytes follow the water. Chloride and bicarbonate ions may have an active transport system at the apical membrane. 4. Immunoglobulin and, possibly, other proteins attach to the basolateral wall of the alveolar cell. They are endocytosed and then transported through the cell to the apical membrane, from which they are released (Neville, March 2001).

2.1.5 Antibodies and other anti-infectious agents in milk

Not only does milk provide the newborn baby with needed nutrients, but it also provides important protection against infection. For instance, multiple types of anti- bodies and other anti-infectious agents are secreted in milk along with the nutrients. Also, several different types of white blood cells are secreted, including both neutrophils and macrophages, some of which are especially lethal to bacteria that could cause deadly infections in newborn babies. (Stabin & Breitz, 2000).

2.1.6 Thyroid scan and the pertechnetate

Nuclear Medicine studies, using gamma rays, provide physiological information. Conventional radiography, CT, US and MRI all provide

anatomical information. The isotope and the carrier used depend on the organ or system to be studied (Frank, 2009).

This means that the Nuclear Medicine image will not necessarily be anatomically recognizable, although in the case of bone scans it often is. A patient who has been injected with a radio-active tracer is slightly radio-active, but the activity is constantly falling, both due to the physical $T^{1/2}$ of the isotope, but also due to breakdown and excretion of the carrier molecules (the biological $T^{1/2}$). The effective $T^{1/2}$ can be defined thus :

$$T^{1/2} \text{ eff} = T^{1/2} \text{ phys} + T^{1/2} \text{ biol}$$

Nuclear Medicine can be used to image most parts of the body, but some organs are imaged much more than other.

For short $T^{1/2}$ isotopes administered in normal diagnostic doses, there is no risk to either the patient or anyone else. It is important to inform the patients of this because they may otherwise worry needlessly, especially as a lot of people equate radiation with atom bombs, Chernobyl, and so on. With most straightforward diagnostic scans, as opposed to therapeutic administration of isotopes, radiation levels are well within the normal variation of background radiation, e.g. watching TV. Patients who have had a diagnostic scan can go near pregnant women or children without causing them any harm, and the same applies after treatment for benign diseases with isotopes such as I^{131} for thyrotoxicosis. Obviously, the patient cannot ask every woman they stand next to if she is pregnant (Frank, 2009).

Some isotopes are excreted via the kidneys and bladder, so in patients suffering from urinary incontinence, care must be taken not to contaminate their bedding, chairs and so on, even with short $T^{1/2}$ isotopes. This is more important when patients are treated with longer $T^{1/2}$ isotopes such as I^{131} (Frank, 2009).

The thyroid is investigated in cases of goitre, or suspicion of hyper- or hypothyroidism .

2.1.6.1 How to perform the nuclear medicine tests

The commonest isotope used is Tc^{99m} as pertechnetate, administered dose 80 MBq. I^{123} as iodide can also be used, administered dose 20 MBq, but is more expensive. The isotope is injected intravenously, and the patient imaged after 15-20 minutes, using a pinhole collimator. If Tc^{99m} is used, there is no special patient preparation and no need to stop anti-thyroid medication such as carbimazole/methimazole or thyroxine. However, these need to be stopped if I^{123} is used. (Frank, 2009)

2.1.6.2 Indications

Goitre

Altered thyroid function

Ectopic thyroid

The thyroid gland lies anteriorly in the neck below the thyroid cartilage Figure (2.2). When thyroid disease is suspected, the first examination is biochemical, looking at the levels of T4, T3 and TSH. The thyroid may be imaged using Ultrasound, CT or Nuclear Medicine tests. The commonest used are Ultrasound and Nuclear Medicine; which one is a matter of preference. Ultrasound will show the size and morphology of the gland, and will identify solid or cystic nodules, and will allow immediate biopsy of solid nodules. On the other hand, a Nuclear Medicine examination shows the function of the gland and differentiates 'hot' from 'cold' nodules. In difficult cases it is probably best to perform both. (Frank, 2009)

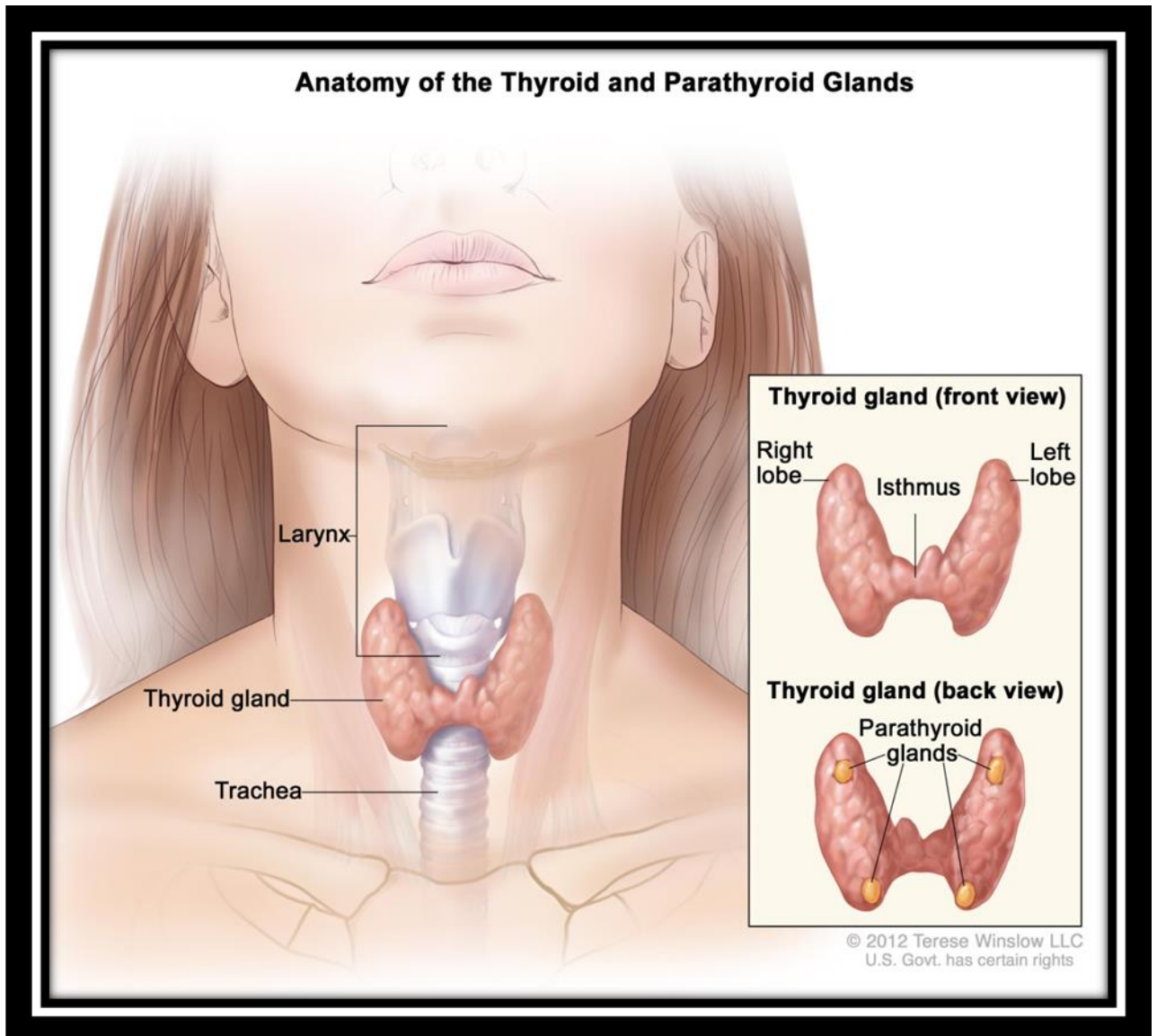


Figure (2.2) position of thyroid gland

2.2 previous studies

(Stabin & Breitz, 2000) stated that, since the content of breast milk varies considerably among different species; therefore we will focus exclusively on measurements from human breast milk when considering the excretion of radiopharmaceuticals. Measurement of breast milk concentrations of radiopharmaceuticals at different times after administration is a relatively easy task, if the patient cooperates in providing the samples. The samples are placed into a well counter or other suitable g counting device and counted with a calibration standard of known activity. For this reason, data on radiopharmaceutical excretion in breast milk have been relatively plentiful. Reports usually include concentrations at several different times after administration of the radiopharmaceutical. By many authors it is notable that concentrations of the administered radiopharmaceuticals in the breast milk may vary over orders of magnitude as reported in different studies involving the same radiopharmaceutical, even in studies in which the same pharmaceutical was administered to the same subject at different times. Per technetate clearly reaches the highest concentrations in breast milk after 3 hours. This suggests that the milk glands handle per technetate like iodide, just as the thyroid gland does.

Mountford and Coakley reviewed data published by various authors and calculated that between 0.13% and 33% of per technetate activities are excreted in milk. But (Rubow, Klopper, Wasserman, Baard, & Neikerk, 1993) thought between 0.56% and 24.4% confirm that widely varying quantities of per technetate are excreted in milk and that very high percentages of the injected activity can follow this route. Only in three patients did the first fraction collected contain the highest concentration of Tc^{99m} . In other cases, peak values

were observed between 1.3 and 8.3 hours after administration of the radionuclide.

Interruption with measurement are recommended as data for these components remain insufficient for generalization. including Tc^{99m} pertechnetate in this category, due to the very large variations between results from different patients. (Rubow, Klopper, Wasserman, Baard, & Neikerk, 1993)

Approximately 55 papers on excretion of radionuclides in human breast milk after radionuclide imaging or therapy have been published. Unfortunately, most of them are case reports or include only a small number of cases. In 1955 the first report was published about a breastfeeding woman after radioiodine treatment of thyrotoxicosis. This early study showed a higher concentration of radioiodine in breast milk than in plasma and investigated the risk to the infant, especially to the thyroid gland. In this issue of the journal, Leide-Svegborn et al. reported data on radioactivity concentrations in breast milk from 53 breastfeeding patients. Their study included one of the largest populations of breastfeeding women studied. The milk was collected at various time-points after administration of 16 different radiopharmaceuticals. The biokinetics of the radiopharmaceuticals using the total fraction excreted in the breast milk and the effective half-life ($T_{1/2\text{ eff}}$) of the radiopharmaceuticals were determined. The absorbed dose coefficients (milligrays per megabecquerel) for organs and tissues and the effective dose coefficients (millisieverts per megabecquerel) for the different radionuclide formulations were calculated using OLINDA/EXM software.

(Rubow et al. 1993) reported data on the excretion of radiopharmaceuticals in human breast milk in 60 patients. An established recommendation for cessation of breastfeeding distinguishes four categories interruption not essential, interruption for a definite period, and interruption with measurement, and

cessation for a longer period. Rubow et al. added a fifth category for those radiopharmaceuticals that have a sufficiently low activity concentration in milk such that no interruption of breastfeeding is required. However, with respect to the radiation exposure to the mother, close body contact between mother and child should be avoided to ensure that the dose to the infant does not exceed 1 mSv. The study by Leide-Svegborn et al. in this issue used only three categories as follows: no interruption, 12-hour interruption, and cessation

However, the issue with ^{99m}Tc -pertechnetate is more complicated. (Leide-Svegborn, Ahlgren, Johansson, & Mattsson, 2015) reported a radioactivity concentration for ^{99m}Tc -pertechnetate of approximately 10 % of the administered activity (%ID) in contrast to a significantly lower %ID for ^{99m}Tc -compounds of approximately 0.05 % for ^{99m}Tc -MIBI to 0.11 % for ^{99m}Tc -HMPAO-leucocytes. From these data a 12-hour interruption after ^{99m}Tc -pertechnetate administration is recommended. The cause of this relatively high concentration of ^{99m}Tc -pertechnetate in breast milk is the presence of a sodium iodide symporter in mammary gland cells, which leads to a significantly higher radioactivity concentration in breast milk than in maternal plasma. The study by Leide-Svegborn et al. showed a lower excretion of radioactivity in breast milk after pretreatment with the thyroid blocking agent perchlorate after Tc^{99m} -pertechnetate administration without blocking a 10 %ID in breast milk was found compared with a significantly lower 0.82 %ID with blocking. These data are supported by animal data from mouse mammary gland cells which also show blocking of the sodium iodide symporter by perchlorate

CHAPTER THREE
MATERIALS AND METHODS

Chapter Three

Materials and Methods

3.1 Materials

3.1.1 Study group

The study was done in Al Nelein Diagnostic Center to a breastfeeding mothers who had undergone thyroid scan using $\text{Na Tc}^{99\text{m}} \text{O}_4$. The sample size was 18 patients.

3.1.2 Equipment

Collecting milk samples was done by manual milk bump.

The volume of the sample was 140ml.

140 ml glass container.

Procedure of dose calibrating done by a dose calibrator

Gamma camera used was Nucline X-Ring-R / Mediso

Multipurpose Single-Head Rectangular and Circular LFOV Gamma Camera for all single head image application with robotic mechanical movements.

Mo-99/Tc-99m Generator - Mallinckrodt

3.2 Methods

3.2.1 Thyroid scan technique

Radiopharmaceutical Administration

Administration of Tc^{99m} Pertechnetate intravenously was done, the dose was 185 MBq. Time interval between administration and scanning was 30 minutes with 30 minutes scanning time.

3.2.1.1 Patient Preparation

Certain thyroid medications interfere with this study. Cytomel (T3) should be discontinued for 2 weeks. Methimazole, and Tapazole should preferably be discontinued for 3 days.

Machine Set-up Instructions: 1. parallel collimator 2. Photopeak and window settings predetermined for Tc^{99m} (140 keV, 15-20%). 3. Preset counts for 200k/anterior image. 4. Mark the sternal notch with a marker.

Scanning Instructions: 1. The patient is supine under the collimator as close as possible with the neck hyperextended. 2. Collect static images of thyroid for 200k counts. 3. Standard view is Anterior with SSN marked.

3.2.2 Measuring of radioactivity in mother's milk

For one patient, four samples were collected after 12, 16, 20 and 24 hours of Tc^{99m} pertechnetate administration with a volume of 140 ml at a time. Then the sample placed at the dose calibrator and the activity had been measured and the readings at different times were registered for 15 different cases.

For another group of patients the readings were measured after 3.5 and 7.5 hours from the injection time.

3.2.3 Methods of data collection

The data collected from text books, web sites, magazines, journals and personal contacts.

3.2.4 Methods of data analysis

Data was analyzed by statistical package for social studies (SPSS), spread sheets, graphs, charts and tables.

3.2.5 Ethical consideration

All data concern to population of the study written by their verbal agreement.

CHAPTER FOUR

RESULT

Chapter Four

Results

Table (4.1) The maximum activity after the administration of $^{99m}\text{TcO}_4$

Patient no.	A* after 3.5 h/140ml	A* after 7.5 h/140ml
1	14.80	4.07
2	15.23	4.22
3	14.88	4.21
Average	14.96	4.16

Table (4.2) Radioactivity in breast milk (MBq/140ml) at different times after administration of $^{99m}\text{TcO}_4$

Patient no.	A* after 12h/140ml	A* after 16/140ml	A* after 20h/140ml	A* after 24h/140ml	% of injected activity
1	0.61	0.30	0.13	0.06	% 10.9
2	0.71	0.40	0.22	0.10	% 11.1
3	0.68	0.38	0.20	0.08	% 11.0
4	0.79	0.44	0.23	0.13	% 11.1
5	0.73	0.40	0.20	0.08	% 11.0
6	0.65	0.34	0.18	0.07	% 11.0
7	0.55	0.27	0.13	0.02	% 10.8
8	0.72	0.41	0.21	0.12	% 11.1
9	0.62	0.33	0.17	0.06	% 10.9
10	0.45	0.13	0.03	0.0	% 10.6
11	0.77	0.45	0.22	0.12	% 11.1
12	0.80	0.46	0.25	0.15	% 11.2
13	0.72	0.39	0.21	0.11	% 11.1
14	0.33	0.10	0.00	0.00	% 10.5
15	0.68	0.38	0.19	0.09	% 11.0
Average	0.65	0.34	0.17	0.07	% 10.96

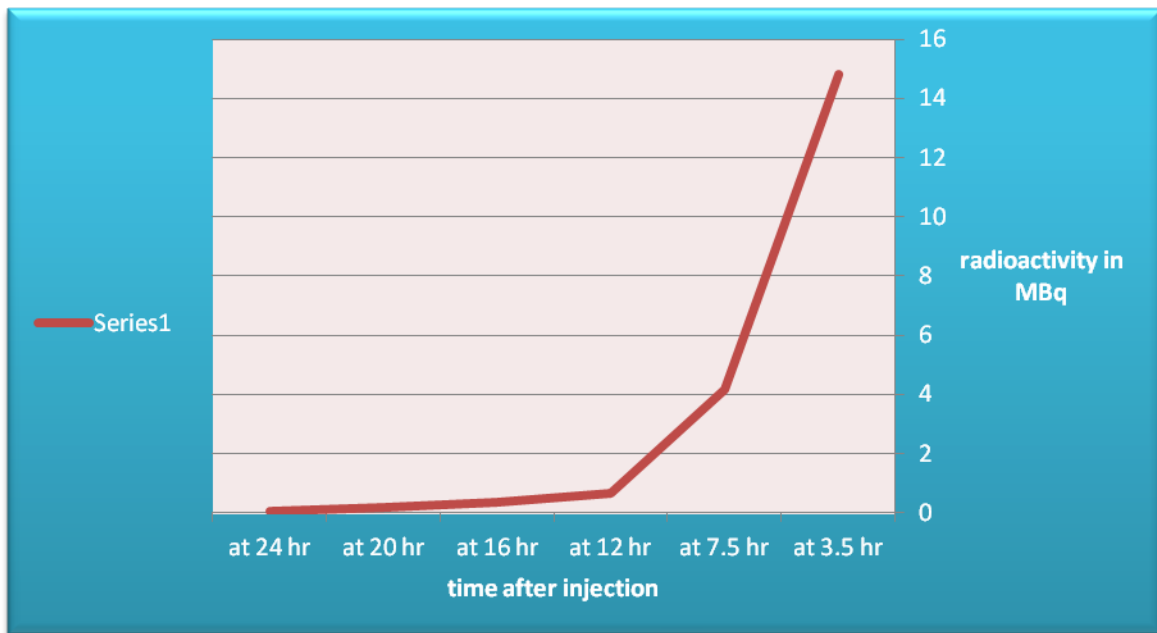


Figure (4.1) line graph represent the measurement of activities in milk at different times

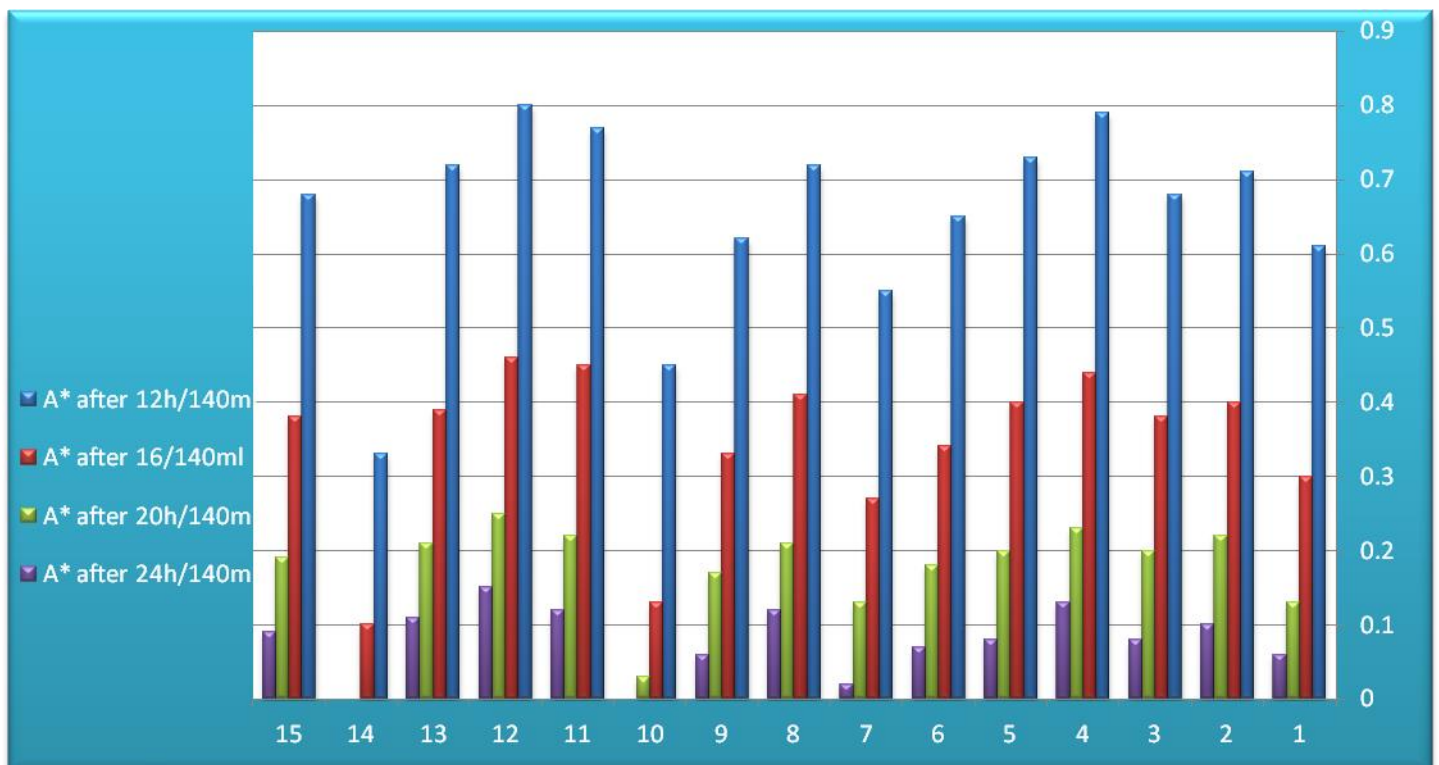


Figure (4.2) Readings of radioactivity in breast milk for 15 patients at different times.

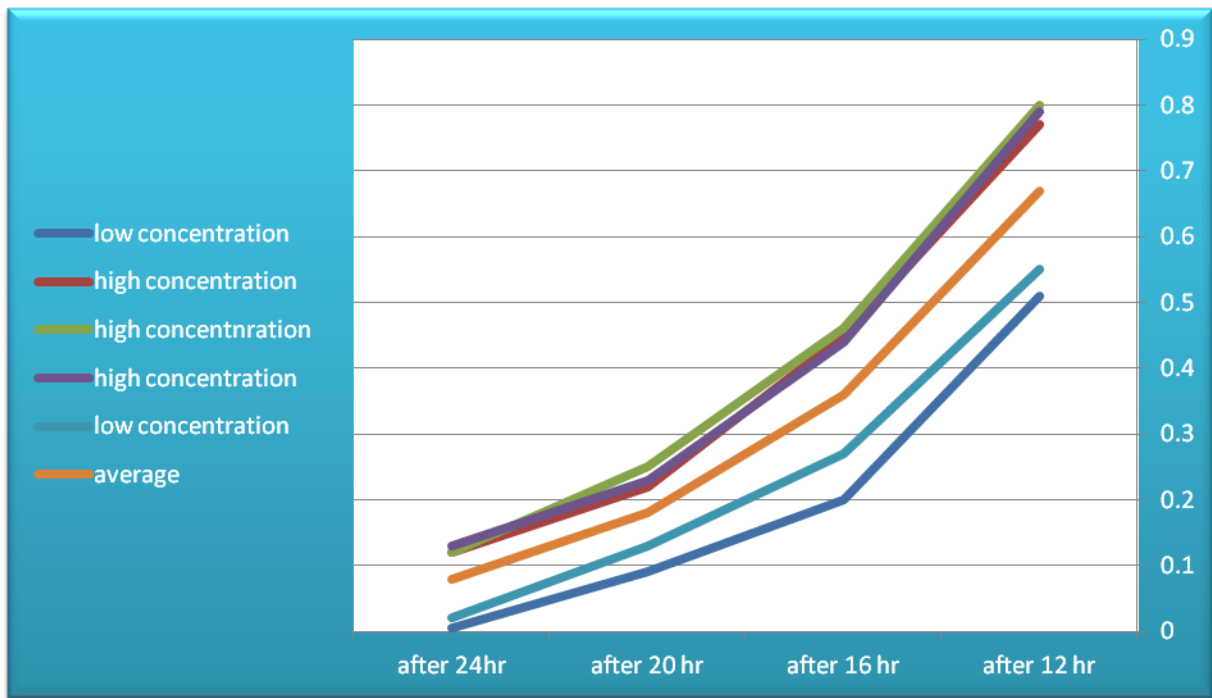


Figure (4.3) Highest and lowest Vs. the average ranges of radioactivity concentration in breast milk.

Table (4.3) Estimation of dose received by the babies.

Patient no.	The estimated dose (in MBq) to the infant after 12hr from the injection	The Effective dose equivalent received by the infant
1	1.1	0.33 mSv
2	1.43	0.429 msv
3	1.34	0.402 msv
4	1.59	0.477 msv
5	1.41	0.423 msv
6	1.24	0.372 msv
7	0.97	0.291 msv
8	1.46	0.438 msv
9	1.18	0.354 msv
10	0.61	0.183 msv
11	1.56	0.468 msv
12	1.66	0.498 msv
13	1.43	0.429 msv
14	0.43	0.129 msv
15	1.34	0.402 msv

CHAPTER FIVE

DISCUSSION, CONCLUSION, RECOMMENDATION

Chapter Five

Discussion, Conclusion, Recommendation

5.1 Discussion

The results obtained from 18 patients were summarized in Table (4.1) and table (4.2). The activity concentrations after different times from administration of the Technetium Pertechnetate in a volume of 140ml represented the fraction of activity excreted in milk from the total administered dose which was 185 MBq.

The possible dose to an infant from ingestion of radiopharmaceuticals was evaluated after 12 hours from the administration of Technetium pertechnetate in 4 hours intervals until 24 hours, in order to estimate the ingested dose as well as the effective dose by the infant. The study assumed that the breast feeding would be resumed after 12 hours instead of the 24 hours period which is adopted presently at the department, during which an amount of 560 ml of milk (140ml every 4 hours) over the next 12hours would be ingested. The total amount of radioactivity that might be ingested by the infant was determined by summing all of the values shown on table 4.3 until the concentrations dropped (as a result of biologic removal or radioactive decay) to negligible values.

In this study, the effective dose (ED), as measured by Mountford and Coakley, to an infant was used. The effective dose equivalent factor used for this study was 0.3 mSv/MBq of the activity ingested by the baby (Rubow, Klopper, Wasserman, Baard, & Neikerk, 1993).

Table (4.1) showed that the highest concentration of activity in milk was found after 3.5 hrs passed from the administration of the $^{99m}\text{TcO}_4$ to the mother (only 3 mothers were involved), then it started to decay according to the effective half life of Tc^{99m} (4.8 hrs) before it was measured again at 7.5 hours.

Table (4.2) demonstrated the data of 15 patients measured at different times after the injection of 128 MBq of $^{99m}\text{TcO}_4$. Measurements of radioactivity were done after 12, 16, 20, 24 hours. The highest readings were 0.80 MBq and 0.79 MBq after 12 hrs as it continued to show the highest readings till 24 hrs from the injection time. The patients who had the highest readings were noticed to have a very low thyroid uptake (e.g. Hypothyroidism). On the other hand the a lower activity readings were 0.45 and 0.55 and it continued to show a lower readings till 24 hours those patients were related to high thyroid uptake (e.g. Hyperthyroidism). The lowest reading was 0.33 but the thyroid uptake was normal, the researcher ascribed that to the age of the baby. Figure (4.2) line graph illustrated the curves of radioactivity concentrations in patients of high and low uptake of thyroid in comparison with the average readings of the activity as described above.

The percentage of the excreted dose in the breast milk was typically estimated to be within the range of 14% to 16% from the injected activity (table 4.2). This value is considerably higher than those reported by Wyburn 1% but it was in the range of (Rubow et al. 1993) results between 0.56% and 24.4% though it considered very wide range. The researcher ascribes the narrow range percentage of excreted dose in milk found in this study to the age approximates of the mothers (30-35 years) as well as the age of the babies (5-12 months) except for one baby whose age was 22 months, despite the thyroid uptake for the mother which was normal, the activity excreted in milk was very low.

Table (4.3) illustrated the sum of activity values (listed previously) that would be ingested by the infant from 12 hours to 24 hours after the injection time. Since the factor of effective dose equivalent to an infant per unit activity administered to the infant is 0.3 mSv/MBq as calculated by (Rubow et al.1993) is factor had been multiplied to the sum of activity values. The cumulative dose,

assuming that feeding started at 12 hours after the injection time, would be simply:

$1.1 \text{ MBq} \times 0.3 \text{ mSv/MBq} = 0.33 \text{ mSv}$. As shown in table (4.3).

The proposed recommendations on breastfeeding interruption were based on an effective dose limit of 1 mSv to the infant, which is the general limit recommended by the ICRP for protection of members of the general public [22] (Leide-Svegborn, Ahlgren, Johansson, & Mattsson, 2015).

The most recent publications recommend that the effective dose equivalent (EDE) to the baby should be kept below 1 mSv (Rubow, Klopper, Wasserman, Baard, & Neikerk, 1993). Therefore, the results showed the breast feeding can be resumed after 12 hours instead of the 24 hours which is the department protocol at the moment.

5.2 Conclusion

In this study, the researcher evaluated the radiation doses of ingested milk by the infants which potentially come from the administration of Tc^{99m} pertechnetate to the mother, in order to estimate the time needed for the $^{99m}TcO_4$ to decay and cleared from the mother's milk. Therefore an exact time can be suggested to resume the breast feeding with minimum radiation dose to the infant. The study can represent a guideline for breast feeding mothers in nuclear medicine centers.

Data in this study presented in tables, charts and line graph in the aim of enabling more practical evaluation of the measurements.

The researcher found that interruption of breast feeding for 12 hours instead of the 24 hours which is adopted by the department, will reduce the ED equivalent to less than 1 mSv which is the general limit recommended by the ICRP for protection of members of the general public. The researcher, therefore, would conclude that breast feeding can be resumed safely at 12 h after administration since it will be difficult for babies specially young infants to stop feeding for long time as the 24 hours. In addition, the researcher results indicated an inverse relationship between thyroid uptake and the amount of radioactivity excreted in the breast milk, as well as a suggested relationship between the age of the baby and the amount of activity excreted. Further researches can be done to correlate between them using more samples. As well as other nuclide investigation rather than thyroid in which Tc^{99m} or other radionuclides are used can be measured in future researches.

5.3 Recommendations

The initial advice is to evaluate the necessity of the examination to the mother, or if it can be postponed or performed using another technique such as Ultra sound.

Depending on the previous results, the researcher recommends resuming of the breast feeding after 12 hours from the injection time instead of the 24 hours which is the current protocol of Al Nelain diagnostic center.

The researcher recommends that when Tc^{99m} pertechnetate is used, the baby should be adequately fed just before the administration of the $^{99m}TcO_4$ and that the next three milk feedings should be suspended. Following this period, breast feeding may be resumed without restrictions. If possible, the mother should be asked to save some milk before the nuclear medicine investigation, which can then be used during the cessation period. Since the interruption of breast feeding will be for 12 hours (as shown by the study), continuous suction of milk is advised to avoid or congestion of milk and hence discomfort to the mother.

Interruption of breast feeding and reduction of nursing time are not the only methods of reducing the total dose to an infant. The activity injected into the mother should be reduced as minimum as possible to get a satisfying diagnostic results.

For other nuclear medicine examinations, the radiopharmaceutical should not be used if high labeling efficiency (radiochemical purity) cannot be achieved, as any radiochemical impurities will result in free pertechnetate which will be excreted in the milk because the milk glands handle pertechnetate like iodide, just as the thyroid gland does.

For other investigations that uses the $^{99m}TcO_4$ like brain scan, thyroid blocking agent should be used as it prevents excretion of the activity in the milk.

Other research studies are recommended with ample period of time and larger sample, to achieve precise and accurate correlation between the thyroid uptake and the age of the baby with the excreted amount of radioactivity in the milk.

The percentage of activity shown earlier can be used as a guideline for different range of activities to predict the exact activity which will be excreted in the milk.

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Appendices

Appendix 1 Manual breast Milk Pump



Appendix2 Gamma camera machine



Appendix3 Dose calibrator

