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MRI Study of the Psoas Major Muscle and its Attachments to the Lumbar Intervertebral Discs: Can a Partial or Absent Attachment of the Psoas to the Disc Trigger Herniation of the Disc?

By Sadaf Batool Faisal, Priyank Gupta, Usama M H Al Bastaki & Claude Pierre-Jerome

Oslo University

Abstract- Background: The Psoas Major muscle attaches to the discs from its origin until the level of L4-L5 disc. It rarely attaches to the L5-S1 disc, and the absence of attachment of the psoas to the L4-L5 disc is frequently seen. Likewise, disc herniation occurs more often at these two lower lumbar discs L4-L5 and L5-S1. Hypothetically, by attaching the disc, the psoas may provide support to the fibrous annulus and prevent herniation of the nucleus pulposus. That may explain the higher incidence of herniation of the lower lumbar discs where the psoas attachment is frequently absent.

Purpose: 1) To search for the location of disc herniation in the lumbar spine, 2) To determine whether the site of the disc herniation coincides with a partial or a total absence of psoas major (PM) attachment to the disc.

Materials and Methods: One hundred and seventy-five magnetic resonance imaging (MRI) lumbar spine examinations from Rashid Hospital, Dubai, UAE were reviewed. There were 89 females, and 86 males, twenty-four East Asians and 151 Arabs, mean age 53.2 (range 21-75) years.

Keywords: psoas major muscle, anatomy, disc herniation, MRI.

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Sadaf Batool Faisal ^α, Priyank Gupta ^σ, Usama M H Al Bastaki ^ρ & Claude Pierre-Jerome ^ω

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The participants were selected by one physician. The inclusion criteria were presence of low back pain, paresthesia, radiculopathy. All selected participants underwent MRI spine examinations. All MRI examinations were performed with the same sequences. The MRI images were read by three Radiologists who were blinded to the clinical examination results such as level of dermatomes and side of symptoms. The location and prevalence of nonattachment of the psoas to the three lower discs were assessed. The association of psoas nonattachment to the disc and disc herniation was calculated using the Pearson Chi Square test with 95% confidence interval (CI), and two-sided p value <0.05 for statistical significance.

Results: At the L5-S1 disc, 16 (9.1%) patients presented with partial attachment of the PM; and 75% of them had disc herniation. One hundred and fifty-nine (90.8%) patients had nonattachment of the PM to the L5-S1 disc; amongst them, 60% suffered from disc herniation. At the L4-L5 disc, partial attachment and nonattachment of the PM to the disc was detected in 77 (44%) patients. Disc herniation was seen in 45 (79.2%) of them. At L3-L4 disc, 12 (6.8 %) patients presented with partial attachment of the PM to the disc. Disc herniation was present in 58.3% of them. The PM's partial attachment and nonattachment to the disc was more common in females at all three disc levels, the highest incidence being at L4-5

level in 60.7% of females compared to 26.7 % of males, $p = .0001$.

There was a higher prevalence of disc herniation at L5-S1 in the older age group (76.1%), compared with the younger age group (52.4%), $p = .003$. The presence of disc herniation associated with nonattachment of the PM muscle to the disc was higher at L4-L5 disc among the younger age group (47.6%) compared with the older age group (23.9%), $p = 0.003$

Conclusions: The partial attachment or nonattachment of the psoas muscle to the lumbar disc may trigger disc herniation with a higher incidence in females and in the younger age group.

Keywords: psoas major muscle, anatomy, disc herniation, MRI.

1. INTRODUCTION

Anatomically, the psoas major (PM) muscle attaches to the lumbar intervertebral discs, to the vertebral bodies and to the transverse processes (1). At the discs level the PM adheres to the fibrous annulus on both sides. In most individuals, the muscle connects to the disc at its anterolateral borders, although it may occasionally extend to the posterior border close to the lateral recess (1,2). Anatomical variants such as partial attachment and nonattachment of the PM to the discs exist; although their prevalence is unknown. Previous reports mentioned the frequent absence of attachment of the PM to the L5-S1 disc and the occasional partial attachment to the L4-L5 disc (3).

The attachment of the PM to the lumbar discs remains enigmatic both from a biomechanical standpoint and from a Radiological perspective. Hypothetically, the PM's attachment to the disc provides support to the fibrous annulus and therefore would prevent extrusion of the nucleus pulposus. Likewise, it can be speculated that the lack of attachment or partial attachment of the PM to the lower lumbar discs L3-L4, L4-L5 and L5-S1, can be a contributing factor in the advent of disc herniation or extrusion. This is a hypothetical thought that has not been thoroughly investigated.

In the general population, the higher incidence of herniation occurs at the lower lumbar discs L4-L5 and

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L5-S1 (4,5), where the nonattachment of the PM muscle is frequent. This can be a cause-effect phenomenon which has not been demonstrated neither biomechanically nor radiologically. The aim of this study is to assess the prevalence of disc herniation in patients with low back pain and search for possible association with the PM muscle's partial attachment or non attachment to the affected disc.

II. MATERIALS AND METHODS

a) Selection of participants and collection of clinical data

This is a retrospective study. The material consists of magnetic resonance imaging (MRI) examinations of the lumbar spine performed from October 2015 to April 2016. The images were retrieved from the picture archiving communication system (PACS) of our Institution. All patients were referred to the Radiological Department by their attending physician because of low back pain of variable duration and paresthesia in the lower extremities originated from the three lower lumbar nerve roots.

During the selection of the material, the criteria set to participate in the study included: a) history of low back pain of long or short duration, b) presence of clinical symptoms - paresthesia, motor deficit, or neurological deficit - suggesting presence of lumbar disc herniation, c) a complete MRI examination of the lumbar spine which included the three lower lumbar discs in axial and sagittal planes. The patients with primary or secondary malignancies, history of trauma, congenital disease affecting the musculoskeletal system such as muscular dystrophy, previous spinal surgery with hardware, history of infection (spondylodiscitis) with destruction of the disc and endplates, were excluded from the study. The demographic data (age, gender, ethnicity), clinical and radiological data of each participant were collected from the electronic Archive system of the same Institution. One hundred and seventy-five patients were selected for the study. Their age ranged from 21 to 75 years, with a mean of 53.8 years. They were 89 females, and 86 males. Among them there were twenty-four East Asians and 151 Arabs. All participants underwent MRI examination of the lumbar spine with the same imaging protocol.

b) MRI examination of the lumbar, sequences and imaging parameters

All selected MR examinations contained images in sagittal and axial planes with cross-sectional slides of at least the three lower lumbar discs from L3 to S1. The images were obtained from a 1.5 Tesla GE imager. The series of images were acquired with the following sequences: a) turbo spin echo (TSE) T1Weighted (T1W) in sagittal plane, b) TSE T2Win sagittal plane, c) short Tau-Inversion Recovery (STIR) in sagittal plane, and d) TSE T2W in axial plane. With a slice thickness of 3

millimeters, a field of view (FOV) of 200, a matrix of 416x288, the number of signal average (NSA) of 1-3, a repetition time (TR)=T1W of 580 milliseconds (ms), T2W (4660ms), STIR(2860ms), echo time (TE)=T1W (11.9ms), T2W(82.19ms), STIR(33.92ms), inversion time (IT) =125, echo train (ET) of T1W =3, of T2W=24, of STIR=12, the examination time would not exceed thirty minutes.

c) Analysis of MR images and assessment of the PM attachment to the disc

The images were analyzed by two experienced Radiologists, as the decisions were reached by consensus. The results were supervised by two senior Radiologists.

The analytic process was three-fold: a) search for disc herniation in the three lower lumbar discs, with emphasis of its location central or lateral, 2) assess the attachment of the PM muscle to both sides of the disc, and verify if the attachment was present, partial, or absent (nonattachment), and 3) verify whether there was disc herniation and partial or absent attachment of the PM muscle to the same disc. To facilitate the assessment of the PM muscle adherence to the disc's borders, and to correctly locate the herniated disc, the disc's surface was divided into four quadrants of equal size. The four quadrants were obtained by drawing two perpendicular lines at the center of the disc (**Figure 1**). The quadrants were named: right anterolateral, left anterolateral, right posterior, and left posterior. When the muscle fascicles adhered to the disc in all four quadrants, it was considered as *complete attachment* (**Figure 1**). The lack of contact of the PM muscle fascicles with the disc border in one, or two, or three quadrants was defined as *partial attachment* (**Figure 2a**). The lack of contact of the PM muscle fascicles to the disc in all four quadrants was defined as total absence of attachment or *nonattachment* (**Figure 2b**).

The PM muscle's attachment to the discs were assessed on the TSE T2W axial images. The presence of lumbar disc herniation was assessed at the last three lower lumbar levels, on both sagittal and axial images. The herniation site was defined as: diffuse, right, central, or left. The disc was considered as herniated when it bulged more than 2 mm from the vertebral margin.

For comparison purposes, the population was sub-classified, based on age, into two sub-groups: group I (21-45 years) and group II (46-75 years). There were two other sub-groups based on gender: male and female; and based on ethnicity: East Asians and Arabs. The data were collected on Excel spread sheets prior to statistical analysis.

d) Statistical analysis

The data was processed with a SPSS software (IBM) version 20 and different categorical variables were tabulated for frequency and percentages separately. For analyzing the association between two categorical

variables we cross tabulated variables and used Pearson Chi Square test to see the significance of association between two variables. With 95% confidence interval (CI), two-sided p value <0.05 was considered statistically significant.

III. RESULTS

a) Prevalence of disc herniation

Out of 175 patients, disc herniation most frequently occurred at L4-5 level in 126 (72%). This was followed by L5-S1 level, in 108 (61.7%) patients; and then by L3-L4 level in 87 (49.7%) patients. The most common patterns of disc herniation and their prevalence at the three disc levels L3-L4, L4-L5, and L5-S1 are presented in **Table I**.

b) Prevalence of PM's partial attachment and nonattachment to the discs associated with disc herniation at the three levels

At the L5-S1 disc level, none of the 175 patients presented with a complete PM attachment to the disc. However, 16 (9.1%) patients presented with a partial attachment of the PM muscle to the disc; while 159 (90.8%) patients had nonattachment of the PM muscle to the disc.

Amongst the 16 patients with PM partial attachment to the disc, 75.0% had disc herniation. From the 159 patients with nonattachment of the PM muscle, 60% suffered from disc herniation (**Figure 3**). Statistically, the difference in the prevalence of disc herniation in patients with partial attachment and those with nonattachment was insignificant, $p=0.371$.

At the L4-L5 disc level, there was the highest prevalence of partial attachment and nonattachment of the PM muscle to the disc. It was seen in 77 (44%) patients. Out of the 77 patients with partial and nonattachment, 45 (79.2%) showed disc herniation (**Figure 4**); compared with 37 (66.3%) patients out of 98 patients with complete psoas attachment and disc herniation, showing a trend of significance, p value = 0.059.

At the L3-L4 disc level, only 12 (6.8 %) patients presented with partial attachment of the PM muscle to the disc. Out of the 12 patients, disc herniation was present in 58.3%, compared with 49.1% patients with complete PM attachment to the disc, which was not statistically significant, P value for Chi Square = .536.

c) Prevalence of side (right / left) of PM muscle partial attachment only at the three discs L3-L4, L4-L5 and L5-S1

When the PM partial attachment to the disc was analyzed separately at each disc level, at L5-S1 disc more patients were seen with partial PM attachment to the right side of the disc compared with the left side, 15 (8.5%) and 7 (4%) respectively.

At the L4-5disc, the PM was partially attached in sixty-seven (38.2%) patients on left side of the disc compared with 63(36%) patients where the PM was partially adhered to the right side of the disc (**Fig.4**).

At the L3-L4 disc level, eight (4.5%) patients had partial attachment of the PM on the left side of the disc; and 8 (4.5%) patients had partial attachment on the right side of the disc.

d) Prevalence of disc herniation and complete PM attachment to the disc at the three levels

At L5-S1 disc level, none of the participants had complete PM attachment to the disc. However, disc herniation was seen in 60.1% of patients with nonattachment of the PM to the disc.

At L4-L5 disc level, disc herniation was observed in 66.3% of patients with complete PM attachment to the disc.

At L3-L4 disc level, disc herniation was seen in 49.1% of patients with bilateral complete PM attachment to the disc.

e) Prevalence of disc herniation in the two age groups, genders and ethnic groups

Based on age, the population was divided into subgroups. There were 104 patients in the younger group (age 21-45 years) and seventy-one patients in the older group, (age 46-75 years).

At L5-S1 disc level, disc herniation was detected in 52.4% of the patients from first age group, compared with 76.1% of patients from older age group, being the difference statistically significant, $p = .003$.

At L4-L5 disc level, among the younger age group of 104 patients, there was a higher prevalence of disc herniation and nonattachment of the PM muscle to the disc, 45 (47.6%) patients compared with 23.9% of patients from the older age group, p value = 0.003.

At L3-L4 disc level, the difference in prevalence of disc herniation between the two age groups was less important. The prevalence was 40.2% in the younger population compared with 58.6% in the older population.

When the two gender groups (female and male) were considered, there was a higher prevalence of disc herniation in females compared to males especially at the level of L4-L5 disc, although not significant. The prevalence of disc herniation in the two age groups, genders and the ethnic groups at all three disc levels is shown in **Table II**.

f) Prevalence of partial attachment and nonattachment in the two age groups, the two gender groups and the two ethnic groups

The analysis of the two age groups revealed a higher prevalence of the PM's partial attachment and nonattachment to the discs in the older population. This difference was more accentuated at the two lower discs. At L4-L5 disc, the partial and nonattachment of the PM

muscle to the disc was seen in 49.3% in the older group compared to 39.8% in the younger group. At L5-S1 disc, the partial and nonattachment of the PM muscle to the disc was detected in 12.7% in the older group compared to 6.8% in the younger group.

When the two genders groups were considered, the PM' spartial attachment and nonattachment to the disc was more common in females compared to males, at all three disc levels. The incidence was highest at L4-5 level, in 54 (60.7%) females, compared to 23 (26.7 %) males, $p = .0001$.

Among the 24 participants from East Asia, 12 (50%) of them presented with partial attachment of the PM to the disc at L4-L5, compared with the Arabs. However, among the 151 Arabs, 11 (7.3%) of them had a partial attachment of the PM at the L3-L4 disc compared with a lower incidence among the East Asians.

The prevalence of PM's partial and nonattachment to the discs in the two age groups, gender groups and ethnic groups is presented in Table III.

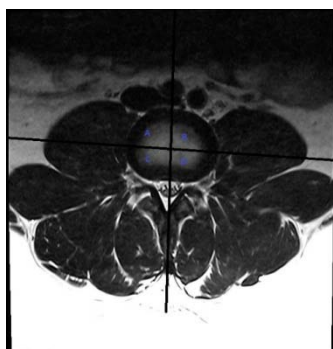


Figure 1: TSE T2W axial image at the level of L4-L5 showing bilateral complete attachment of the psoas major muscle to the intervertebral disc in the four quadrants divided by drawing two perpendicular lines at the center of the disc.

A: Right anterolateral; B: Left anterolateral; C: Right posterior; D: Left posterior

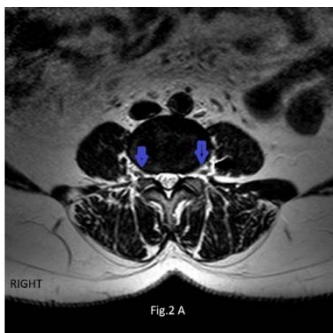


Figure 2A: TSE T2W axial image at L4-L5 level showing bilateral partial attachment of the psoas major muscle to the disc. Attachment of the muscle is absent in right and left posterior quadrant (arrows). There is no disc herniation.



Figure 2B: TSE T2W axial image at L5-S1 level showing nonattachment of the psoas major muscle to the disc (arrow). There is no disc herniation. Note the variant small psoas on the left.

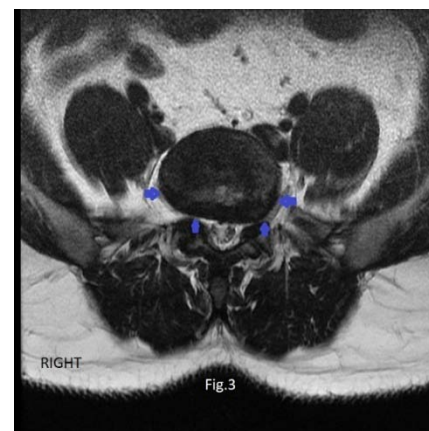


Figure 3: TSE T2W axial image at L5-S1 level showing nonattachment of the psoas major muscle to the disc associated with a circumferential disc herniation (arrows).

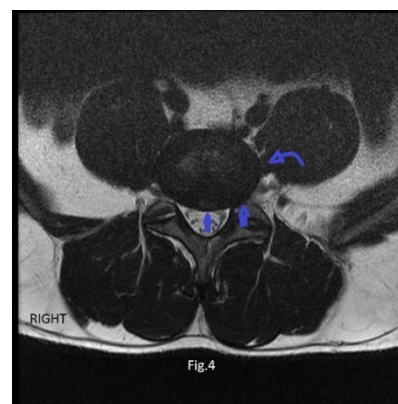


Figure 4: TSE T2W axial image at L4-L5 level showing complete attachment of the psoas major muscle to the disc on the right side. There is partial attachment of the psoas major muscle to the disc on the left side (curved arrow) with absence of muscle fiber attachment in left posterior quadrant. A central and left posterolateral disc herniation is noted (arrows).

Table I: Prevalence and distribution of the three common patterns of disc herniation at the three levels L3-L4, L4-L5 and L5-S1 in the 175 participants

LEVELS	Circumferential Herniation Nos (%)	Central Herniation Nos (%)	Paracentral Herniation Nos (%)	Total Nos (%)
L3-L4	78 (44.5)	3 (1.7)	5 (2.8)	86 (49.1)
L4-L5	117 (66.8)	8 (4.5)	3 (1.7)	128 (73.1)
L5-S1	86 (49.1)	15 (8.5)	7 (4.0)	108 (61.7)

Table II: Prevalence of disc herniation in the two age groups, genders and the ethnic groups at all three disc levels.

LEVELS	21-45 YEARS	46-75 YEARS	MALES	FEMALES	EAST ASIANS	ARABS
L3-L4	34.1%	71.8%	40.7%	58.4%	41.7%	51.0%
L4-L5	62.1%	85.9%	69.8%	74.2%	70.8%	72.2%
L5-S1	52.4%	76.1%	65.1%	58.4%	66.7%	

Table III: Prevalence of PM's partial and nonattachment to the discs in the two age groups, genders and ethnic groups

LEVELS	21-45 YEARS	46-75 YEARS	MALES	FEMALES	EAST ASIANS	ARABS
L3-L4	3.9%	11.3%	2.3%	11.2%	4.2%	7.3%
L4-L5	39.8%	49.3%	26.7%	60.7%	50.0%	43.0%
L5-S1	6.8%	12.7%	8.1%	10.1%	16.7%	7.9%

IV. DISCUSSION

On magnetic resonance (MR) cross-sectional images, the PM muscle emits a moderate signal intensity compared to other muscles. The sagittal images are less useful to evaluate the PM, while the axial slices permit a fair appreciation of the PM's attachment to the lumbar intervertebral discs and the anatomical variants. In this study, the authors aimed to analyze the relationship between the pattern of attachment and nonattachment of the PM to three lumbar disc and the possible impact on the herniation of the disc.

In previous studies, several conditions such as abnormal posture (6), increased intradiscal pressure (7,8) have been mentioned as causative factors of lumbar disc herniation. The partial attachment or nonattachment of the PM to the disc had not been considered as possible influential factors to disc herniation. Neither the differences in the prevalence of these anatomical variants with regards to demographics have been subject to investigation. Hypothetically, we postulated that individuals with anatomical variations of the PM attachment to the disc may suffer from a higher risk of herniation, assuming the PM's attachment to the disc would provide support to the fibrous annulus and therefore prevent annulus tear and extrusion of the nucleus pulposus.

At the L4-L5 disc, we found the highest prevalence of partial attachment and nonattachment of the PM muscle to the disc in 77 (44%) patients. Of them, 45 (79.2%) suffered with low back pain and disc herniation. This finding pointed toward a possible cause

and effect phenomenon that has not been previously considered. In our study, a population of 175 subjects was evaluated. The highest prevalence of disc herniation (72%) was detected at L4-L5 level, which concurred with previous reports (4,5,8).

The PM's nonattachment to the L5-S1 disc has previously been reported (8,9), and considered as anatomically normal, since it occurs in most individuals. In our study, the nonattachment was seen in 159 (90.8%) subjects with a high prevalence of herniation (60% of them). Of the rest -16 (9.1%) subjects-, who presented with PM's partial attachment, 75% had disc herniation. Such high occurrence of disc herniation at the two lower discs and the high prevalence of the PM's partial and nonattachment to the disc may be related.

From the study's results, the demographic factors - age and gender- seemed to have some influence on the advent of disc herniation in individuals with partial or nonattachment of the PM to the disc. We found that a higher frequency of disc herniation at L4-L5 level and L5-S1 level in the younger individuals with partial or nonattachment of the PM to disc. The difference in prevalence was more accentuated at L4-L5 disc, 47.6% versus 23.9% with statistical significance ($p=0.003$). This further emphasizes the role of muscle attachment pattern in inducing herniation of the disc, with a possible stronger influence among younger subjects.

Also, a significant association between the PM's muscle nonattachment to the disc and disc herniation was found with a higher frequency in females (60.7%) compared to males (26.7%), especially at the L4-L5 disc. This difference has not been described previously.

The selected population was represented by two different Ethnic groups: Eastern Asians (24 subjects) and Arabs (151 subjects). Because of the discrepancy in the numbers (24 versus 151) no significant comparative data could be obtained for the two ethnic groups; which constitutes a limitation of the study.

A study with a larger population with larger diverse ethnic groups may be necessary to better understand the correlation between ethnicity, PM's attachment to the disc and disc herniation. Likewise, the statistical difference between genders and different age groups for PM's attachment to the disc and disc herniation deserve further investigation. To our knowledge, no previous study had focused on the PM muscle attachment to the disc as a possible contributing factor in disc herniation in relation with demographics.

In conclusion, the PM muscle's partial attachment and nonattachment to the lower lumbar discs may be a triggering factor for initiating disc herniation especially in younger age groups and in females. Further prospective studies with larger population are needed to confirm this hypothesis.

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Effect of Socio-Demographic Factors, Family Information and Gynecology History on Ultrasound Breast Morphology in Different Age Groups

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Abstract- Background: A number of factors such as age, hormones, reproductive history, diet and genetics influence the morphology of a woman's breast. A study conducted found age, hormones, reproductive history, genetics and diet (body habitus) to be the major contributors to breast density. The purpose of this study was to assess knowledge and find association of breast morphology with socio-demographic factors, family information and gynecology history by ultrasound.

Methods: A self-administration questionnaire that included information of patients and an analytic cross-sectional study design was used to determine the morphology of normal breast among all respondents that attending the imaging department of Golden Horses Health Sanctuary, Sri-Kembangan located in Klang Valley, Selangor, Malaysia. All women were subjected to bilateral whole breast ultrasound using ultrasound.

Keywords: breast morphology, ultrasound, age, ethnic, socio-demographic factors, marital status.

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Effect of Socio-Demographic Factors, Family Information and Gynecology History on Ultrasound Breast Morphology in Different Age Groups

Shahad A Ibraheem ^α, Rozi Mahmud ^σ, Suraini Mohamad Saini ^ρ, Norafida Bahari ^ω & Mousa Alazzwi [✱]

Abstract- Background: A number of factors such as age, hormones, reproductive history, diet and genetics influence the morphology of a woman's breast. A study conducted found age, hormones, reproductive history, genetics and diet (body habitus) to be the major contributors to breast density. The purpose of this study was to assess knowledge and find association of breast morphology with socio-demographic factors, family information and gynecology history by ultrasound.

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Results: About 615 women were examined from October 2013 to December 2014 within age groups from 20-70 years old and different ethnic group (Malay, Chinese and Indian). The majority of mean age were 45.92, the mean of menopausal of premenopausal age was 43.00(SD5.54), while for post-menopausal age was 49.79(SD3.53). Studies were equal among age groups, religion, education level, occupation, income and marital status and some tissue in different quadrant for right and left breast i.e subcutaneous fat of left breast in UOQ (L=0.48, p-value=0.75), LOQ (L=1.82, p-value=0.13) and UIQ (L=1.27, p-value=0.24).

Conclusion: Study shows that there was variation and association in tissue with age, ethnic and religion in different quadrants with p-value > 0.05, except in some quadrant of other tissue of right and left breast quadrants, while in education level, occupation, income and marital status there were no association with breast morphology.

Keywords: breast morphology, ultrasound, age, ethnic, socio-demographic factors, marital status.

1. INTRODUCTION

The breast which is primarily influenced by the endocrine system serves as a secondary sex organ in humans and also possesses the ability to produce milk in mammals. With these vital functions of the breast, it is important for the radiologist to understand the normal anatomy and physiology of the breast in order to be able to identify abnormalities which may occur in any breast [1]. The major anatomical structures in the breast include skin, fat, facial layers, Cooper ligaments, fibro glandular tissue, lymphatic, and neurovascular structures, which are all placed over the chest wall. The volume of fibro glandular tissue in women differs with age, with many women having more fat within the breasts after menopause [2]. Breast ultrasound plays a major role in the identification, diagnosis, and staging of breast cancer [3,4]. At present, it is generally assumed that glandular tissue, which is a common site for breast cancer, is the most vulnerable among the tissues (adipose, skin, and areolar tissues) making up the breast [5]. The amount of glandular tissue is linked to breast cancer risk, so an objective quantitative analysis of glandular tissue can aid in risk estimation [6]. Based on the study, the morphology of breast using ultrasound assessment suggesting that in young non lactating breast, the tissue is primarily composed of fibro glandular tissue with little or no subcutaneous fat. With increasing age and parity, fat is deposited in both the subcutaneous and retro mammary layers [7]. The difference in incidence rates between the Malays and Chinese can be explained in terms of the risk factors e.g. Increasing age, geographic location, family history, reproductive factors, oral contraceptives, Hormone replacement therapy and more, known to be associated with breast cancer. There is also a possibility of under-reporting in Malay women because they are more likely to seek alternative therapy and hence not present to the medical practitioner [8]. The main reason for conducting this study is to reduce breast cancer percentage in Malaysia by early detection of abnormalities which may lead to cancer, and that can be done by referencing the diagnosis of

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normality and its measurements in different age and ethnic groups.

II. PATIENTS AND METHOD

a) Study design and population

Analytic cross-sectional research design was conducted from October 2013 to December 2014 on females admitted to the imaging department of Golden Horses Health Sanctuary (GHHS) for breast checking in Seri Kembangan district located within Klang Valley, Selangor, Malaysia. Respondents were identified and selected using modest random sampling method. Subjects were randomly selected from the list of respondents that went to the Imaging Department in the GHHS using SPSS. This list was used as sample frame. A total of 615 females were selected.

b) Data collection

Data was collected using self – administered questionnaires which was developed and validated especially for this study. All women subjected to bilateral whole breast ultrasound examination using Philips ultrasound iu22. Both breasts were scanned utilizing clockwise, overlapping radial approach. The breast divided into four quadrants. Each quadrant was scanned in a radial fashion to accommodate the arrangement of ducts in the breast with a linear array probe L17-5 (5-17MHz), depth 3.5-4.0 cm and gain 86%-87%. Data are acquired at the region of interest (ROI).

c) Inclusion Criteria

The inclusion criteria for normal breast respondents were females aged 20 to 70 years.

d) Exclusion Criteria

- A. Male
- B. Females < 20 years old because permission was needed from parents
- C. Females > 70 years old because no obvious changes occurred on breast
- D. Women that used contraceptive pills or device.
- E. Women that used hormone replacement therapy.
- F. Women with history of breast diseases such as:
 - i. *Benign breast tumors*: fibrosis or cysts and fibroadenoma or intraductal papilloma are abnormal growths which caused a change in the breast tissues.
 - ii. *Malignant breast tumors*: carcinoma, adenocarcinoma, carcinoma in situ, invasive carcinoma and sarcoma are types of breast cancer that grow in glandular tissue and breast duct.
 - iii. Breast infections such as mastitis occurred frequently during breast feeding.
 - iv. Nipple infections, mammary duct ectasia and intraductal papilloma caused nipple discharge.

e) Ethical consideration

Ethical approval to conduct the study was obtained from medical research ethnics committee of the Universiti Putra Malaysia. Then approval was obtained from The Medical Research and Ethics Committee, Ministry of Health - Malaysia. A written consent was taken from each respondent before conducting the survey.

f) Statistical analyses

All analyses were performed using SPSS[®] software, version 21.0 (SPSS Inc., Chicago, IL, USA). Normality test were done and all of the quantitative data were found to be normally distributed. Descriptive statistical analysis, which included frequency, mean and standard deviation (SD), was used to characterize the data. Parametric test (one-way ANOVA and t-test) and non-parametric test (Kruskal Wallis and Mann-Whitney) employed to determine the association between normal breast morphology and socio-demographic factors, family information and gynecology history. The level of statistical significance was set at $\alpha < 0.05$.

g) Breast image analysis

For measuring and analyzing the breast tissues, Philips DICOM Viewer software (R 3.0- SP03) was used. The measuring unit for each tissue is (mm), and the dimensions were obtained. Furthermore, all the measured data were collected by uni-dimensional (length) for subcutaneous fat while two-dimensional (length \times width) for glandular tissue and fat lobules, sizing from three different areas for each tissue three readings were taken and average obtained to minimize errors.

III. RESULT

Total of 700 respondents were selected as sample for this study. However 85 respondents (12.14%) returned questionnaires were omitted due to either incomplete answers or were inaccurately completed. Hence, 615 females participated in this study were counted. The giving response rate in this study was 87.9%.

a) Factors associated with performing US on breast morphology

Table 1 shows the distribution of respondents according socio-demographic factors (age, race, religion, education level, occupation, and income), family information (marital status), and gynecology history (menarche age, menopause age and family history of breast cancer). Overall, the majority of mean age were 45.92 (SD= 12.94), Chinese 326(51.4%), Buddhism 282(45.9%), having degree 114 (18.5%), most of them working 209(60%), having income rang 1001-3000RM, married 538(87.5%), the mean of first menstrual cycle was 12.1(SD0.64), the mean of menopausal of premenopausal age was 43.00(SD5.54),

while for post-menopausal age was 49.79(SD3.53) and 46(7.5%) of respondents reported having a family history of breast cancer.

Table 1: Socio-demographic data of respondents (n=615)

Characteristics	Frequency	Percent (%)	Mean±SD
Age groups			45.92 ± 12.94
20-29	78	12.7	
30-39	137	22.3	
40-49	112	18.2	
50-59	184	29.9	
60-70	104	16.9	
Ethnicity			
Malay	203	33	
Chinese	326	51.4	
Indian	96	15.6	
Religion			
Muslim	208	33.8	
Christian	40	6.5	
Buddhism	282	45.9	
Hinduism	85	13.8	
Educational level (n=237)			
Primary/ secondary	28	4.6	
Diploma	82	13.3	
Degree	114	18.5	
Postgraduate	13	2.1	
Employment status (n=349)			
Student	25	7.2	
Working	209	60	
Housewife/retiree	115	32.4	
Income (n=221)			
<1000	7	3.2	
1001-3000	105	47.5	
3001-5000	94	42.5	
>5000	15	6.8	
Marital status			
Single	75	12.2	
Married	538	87.5	
Widower	2	0.3	
Age of first menstrual			12.1 ± 0.64
Menopausal age			
Premenopausal age			43.00 ± 5.54
Postmenopausal age			49.79 ± 3.53
Family history of breast cancer			
Yes	46	7.5	
No	569	92.5	

Data presented as mean ± SD for age groups

The percentage of participants who performed Ultrasound was 615 (100%). Among those who did ultrasound wide range of breast tissue size founded.

As shown on Table 2 and Table 3 the relationship between breast morphology and socio demographic parameter, family information and gynecology history. In each quadrant of the breast, the distribution varied between normal and non-normal. For analyzing normal data one-way ANOVA and t-test was used to find the association between breast morphology and socio demographic factors, marital status and breast cancer history after using homogeneity test of

variance, and according to that test plus Levene statistics, variances were equal among age groups, religion, education level, occupation, income and marital status and some tissue in different quadrant for right and left breast i.e subcutaneous fat of left breast in UOQ (L=0.48, p-value=0.75), LOQ (L=1.82, p-value=0.13) and UIQ (L=1.27, p-value=0.24) respectively. For non-normal data, nonparametric test of Kruskal Wallis and Mann-Whitney was used. At the current study, there was

variation and association in tissue with age, ethnic and religion in different quadrants with p-value > 0.05, except in some quadrant of other tissue of right and left

breast quadrants, while in education level, occupation, income and marital status there were no association with breast morphology.

Table 2: Association between right breast morphology and socio demographic in different quadrants for normal and non-normal distribution

Breast morphology	Socio demographic factors											
	Age				Ethnic				Religion			
	F	P-value	χ^2	P-value	F	P-value	χ^2	P-value	F	P-value	χ^2	P-value
Subcutaneous fat												
Upper outer	23.62	0.000*										
Lower outer	25.46	0.000*			8.47	0.000*			6.48	0.000*		1.34 0.260
Lower inner			65.8	0.000*	11.99	0.000*			7.20	0.000*		4.81 0.003*
Upper inner	24.4	0.000*			12.40	0.000*			7.76	0.000*		3.53 0.016*
							13.11	0.001*			12.26	0.007* 3.23 0.023*
Glandular tissue												
Upper outer	3.82	0.004*			19.48	0.000*			13.62	0.000*		2.44 0.065
Lower outer			14.52	0.006*	17.12	0.000*			11.57	0.000*		1.91 0.129
Lower inner			14.12	0.007*	6.68	0.001*			5.21	0.001*		2.82 0.039*
Upper inner			14.57	0.006*	14.60	0.000*			9.38	0.000*		1.20 0.310
Fat lobules												
Upper outer			12.64	0.013*	27.13	0.000*			19.03	0.000*		2.41 0.067
Lower outer			11.58	0.021*	36.56	0.000*			23.56	0.000*		2.82 0.04*
Lower inner			9.83	0.043*	38.12	0.000*			26.19	0.000*		1.99 0.12*
Upper inner			13.49	0.009*	30.68	0.000*			22.35	0.000*		2.23 0.085

*significance value at level $p < 0.005$

Breast morphology	Socio demographic factors											
	Occupation				Income				Marital status		Breast cancer history	
	F	P-value	χ^2	P-value	F	P-value	χ^2	P-value	F	P-value	t	P-value
Subcutaneous fat												
Upper outer	14.51	0.000*										
Lower outer			33.52	0.000*	2.24	0.084			1.34	0.260	-1.23	0.137
Lower inner			24.14	0.000*	2.87	0.037*			4.81	0.003*	-1.11	0.869
Upper inner	10.21	0.000*			4.62	0.004*			3.53	0.016*	-0.63	0.335
					3.95	0.009*			3.23	0.023*	-0.85	0.847
Glandular tissue												
Upper outer	1.53	0.22			1.76	0.16			2.44	0.065		
Lower outer	1.48	0.23			1.66	0.18			1.91	0.129	-0.49	0.037*
Lower inner			4.65	0.098			10.43	0.02*	2.82	0.039*	-1.54	0.031*
Upper inner	1.78	0.17			0.58	0.63			1.20	0.310	0.58	0.319
											-0.76	0.011*
Fat lobules												
Upper outer	2.90	0.057			2.49	0.061			2.41	0.067	0.23	0.869
Lower outer	5.10	0.007*			3.37	0.019*			2.82	0.04*	-1.02	0.575
Lower inner	7.86	0.000*					2.07	0.56	1.99	0.12*	0.12	0.897
Upper inner	3.15	0.044*			1.52	0.21			2.23	0.085	-0.73	0.064

*significance value at level $p < 0.005$

Table 3: Association between left breast morphology and socio demographic in different quadrants for normal and non-normal distribution

Breast morphology	Socio demographic factors											
	Age			Ethnic			Religion			Education level		
	F	P-value	χ ²	P-value	F	P-value	χ ²	P-value	F	P-value	χ ²	P-value
Subcutaneous fat												
Upper outer	8.66	0.000*										
Lower outer	5.51	0.000*		7.61	0.001*		19.14	0.000*	3.85	0.010*		
Lower inner			7.33	0.000*		17.95	0.000*	6.69	0.000*	3.68	0.013*	
Upper inner	4.19	0.002*				33.91	0.000*		3.09	0.028*		
						15.22	0.000*		2.92	0.035*		
Glandular tissue												
Upper outer												
Lower outer			68.41	0.000*	28.04	0.000*	19.43	0.000*	4.05	0.008*		
Lower inner			31.84	0.000*	22.12	0.000*	14.08	0.000*	3.07	0.029*		
Upper inner			26.61	0.000*	16.05	0.000*	11.64	0.000*			10.08	0.018*
			47.37	0.000*	24.90	0.000*	17.56	0.000*	3.59	0.014*		
Fat lobules												
Upper outer			24.85	0.000*	27.36	0.000*	17.22	0.000*	0.93	0.430		
Lower outer			40.27	0.000*	31.78	0.000*	19.79	0.000*	4.01	0.008*		
Lower inner			69.59	0.000*	26.68	0.000*	18.39	0.000*	1.73	0.160		
Upper inner			46.77	0.000*	30.09	0.000*	18.31	0.000*	2.21	0.087		

*significance value at level p<0.005

Breast morphology	Socio demographic factors											
	Occupation				Income				Marital status			
	F	P-value	χ^2	P-value	F	P-value	χ^2	P-value	F	P-value	χ^2	P-value
Subcutaneous fat												
Upper outer	9.61	0.000*		3.26	0.02*				9.98	0.000*		
Lower outer	13.14	0.000*		4.47	0.005*				10.41	0.000*		
Lower inner	19.84	0.000*		4.10	0.007*				13.47	0.000*		
Upper inner	13.37	0.000*		6.03	0.001*				9.87	0.000*		
											13053.5	0.977
Glandular tissue												
Upper outer			9.50	0.009*								
Lower outer	1.35	0.26					6.82	0.078			1.92	0.38
Lower inner	2.27	0.11		1.14	0.34						5.02	0.081
Upper inner	0.83	0.44					6.75	0.08			5.88	0.05*
				2.41	0.07						0.35	0.84
Fat lobules												
Upper outer	0.96	0.38					2.49	0.48			5.10	0.078
Lower outer			11.74	0.003*			5.66	0.13			4.06	0.13
Lower inner	3.72	0.025*		1.52	0.21						6.76	0.034*
Upper inner	2.77	0.064					9.91	0.02*			3.84	0.15

*significance value at level $p < 0.005$

IV. DISCUSSION

Aging of human breast tissue is often followed by particular structural and functional changes and these changes have been linked by several research findings to the development of aging-related cancer. At the cellular level, morphological and functional changes which may include increased cell size and decreased proliferation may result in aging of human mammary epithelial cells [9]. The development of the breast begins from the stage of fetal development with mammary ridge or milk line which is usually a thickening in the chest region after which the nipples and milk duct system begin to develop when the baby is born, then at puberty stage, child-bearing phase, during menstrual cycle and finally at menopause [10].

In the present study the finding is consistent as in other studies which linked age with breast changes [11, 12]. Our work confirms that an increase in age is associated with a reduction in glandular tissue. Moreover the increment of fat in the breast and the radiographic appearance of the breast vary among women of the same age because of variations in breast tissue composition [13]. Most of the studies done in Malaysia, focused on the knowledge of breast cancer screening using mammography or breast self-examination with socio demographic factors such as [14-16]. These studies have similar findings of the association of women with ethnicity, religion, occupation, income, marital status, degree level of education. Family history of breast cancer was higher than those with secondary or primary level of education ($p < 0.001$). Only a few studies have reported on the variation of breast density by race, however, one study done in Department of Imaging, Country Height Health Sanctuary, Malaysia With the total number of 610 subjects, there were significant associations between breast density and age group and there were no significant association with ethnic groups [17-20]. This is important, because different racial/ethnic groups have different breast cancer risk and these differences change with age [21]. Furthermore, some studies found higher breast cancer risk among women with professional occupations such as nursing [22] and teaching [23-26]. A study by Rubin et al., (1993) found teachers to be twice at risk of breast cancer mortality compared to other women. Although marital status have been commonly identified by various studies [27-30] as a positive factor in early cancer diagnosis and better survival, local studies [31,32] to date have not established any significant relationship between marriage and uptake of breast cancer screening. However, there was a study among female secondary school teachers from 20 selected secondary schools in Selangor, Malaysia to determine the knowledge and practices on breast cancer screening and socio demographic but there was no significant knowledge

[33]. Yet no studies have been carried out on normal breast morphology related to the socio demographic factors using ultrasound.

V. LIMITATION

As this study was designed to be cross-sectional. It may not be possible to conclude that the factors were found to be associated with normal breast morphology predated onset. Incidentally all the respondents that were selected from GHHS which is located in urban area; hence, the result cannot be generalized to both urban and rural.

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Differences in Contrast-Enhanced CT Features between Clear Cell Renal Carcinoma and Non- Clear Cell Renal Carcinoma

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Materials and methods: We retrospectively analyzed 64 patients (39 clear cell and 25 non clear cell) of renal cell carcinoma (RCC) from February, 2014 to February, 2016. We excluded 2 cases of angiomyolipoma and one case of oncocytoma because of their benign characteristics. So, total number of non- clear cell renal carcinoma was 22. Two radiologists retrospectively reviewed CT studies in an independent and blinded fashion. We compared Patient age and sex; tumor size; margin (clear or ill defined); location; presence or absence of hemorrhage, necrosis, calcification; degree of enhancement (hypodense, isodense or hyperdense); pattern of enhancement (homogenous or heterogeneous); tumor spreading pattern including presence or absence of thrombus (inferior vena cava and renal vein), lymphadenopathy, ascites. We performed statistical analysis with the help of SPSS 17.1 Software.

Keywords: *contrast enhanced CT; clear cell RCC (ccRCC); non clear cell RCC (Non-ccRCC).*

GJMR-D Classification: *NLMC Code: QT 34*



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Differences in Contrast-Enhanced CT Features between Clear Cell Renal Carcinoma and Non-Clear Cell Renal Carcinoma

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Abstract- Purpose: Different RCC has different behavioral characteristics and their management protocol also different. Our purpose was to differentiate clear cell renal carcinoma from Non clear cell renal carcinoma with the help of contrast enhanced CT imaging features, which might help the clinician to make early decision about the management of renal cell carcinoma.

Materials and methods: We retrospectively analyzed 64 patients (39 clear cell and 25 non clear cell) of renal cell carcinoma (RCC) from February, 2014 to February, 2016. We excluded 2 cases of angiomyolipoma and one case of oncocytoma because of their benign characteristics. So, total number of non- clear cell renal carcinoma was 22. Two radiologists retrospectively reviewed CT studies in an independent and blinded fashion. We compared Patient age and sex; tumor size; margin (clear or ill defined); location; presence or absence of hemorrhage, necrosis, calcification; degree of enhancement (hypodense, isodense or hyperdense); pattern of enhancement (homogenous or heterogeneous); tumor spreading pattern including presence or absence of thrombus (inferior vena cava and renal vein), lymphadenopathy, ascites. We performed statistical analysis with the help of SPSS 17.1 Software.

Results: In corticomedullary phase, most of Clear cell RCC 21 of 39 (53.8%) tended to show hyperdense enhancement, whereas, most of non- clear 21 of 22 (95%) showed hypodensity and only 1 of 22 (5%) showed isodensity. When, we compared homogeneity and heterogeneity in between two groups, we found non- clear RCC_s (86%) were more heterogeneous than clear cell RCC_s (53%) ($P < 0.05$). ccRCC 15 of 39 (38.5%) usually located in middle pole whereas most of non- clear cell RCC 15 of 22 (68.2%) did not show any specific polarity predilection ($P < 0.05$). 33 of 39 (84.6%) ccRCC involved medulla, whereas 20 of 22 (90.9%) non clear cell RCC showed mixed involvement of cortex, medulla and pelvis but no specific tendency to locate ($P < 0.05$). Calcification was more common in non-clear cell RCC (27.2%) than ccRCC (7.6%).

Conclusions: Contrast enhanced CT provides reliable information for differentiating clear cell RCC and non-clear cell RCC. Degree and pattern of enhancement is the most important parameter but presence or absence of calcification, necrosis and location also have supplementary values.

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Keywords: contrast enhanced CT; clear cell RCC (ccRCC); non clear cell RCC (Non-ccRCC).

1. INTRODUCTION

Renal cell carcinoma (RCC) accounts for more than 2% of cancers in humans worldwide [1,27]. It is the seventh most common malignancy in male and 12th most common malignancy in female [2, 28]. Many researchers have stated that renal cell carcinoma (RCC) is not a single disease but rather, a group of several disease entities [3,4,10]. In 2004 WHO classified RCC into different histopathologic types which is showed in table 1:

Table 1: 2004 World Health Organization Classification of RCC

Clear cell (conventional) RCC
Multi locular clear cell RCC
Papillary RCC
Chromophobe RCC
Carcinoma of collecting ducts of Bellini
Renal medullary carcinoma
X _p 11 translocation carcinoma
Carcinoma associated with neuroblastoma
Mucinous tubular spindle cell carcinoma
Unclassified RCC
Source-Reference 30

The classification of renal cell carcinoma into subtypes has become of interest because of the association with prognosis [10]. Different tumor behavior and aggressiveness related to histologic subtypes and some others well- established parameter according to Fuhrman grade (tumor size and stage) [6,7,27]. Clear cell carcinoma also known as conventional renal carcinoma is the most common subtype, accounting for 65% of RCC [8,9]. Papillary and chromophobe renal carcinoma comprise 25% of RCC [8,9]. Collecting duct is a rare subtype, accounting for less than 1% of all RCC [5]. Patients with papillary renal carcinoma or with chromophobe renal carcinoma have a higher 5- year survival rate than those with conventional renal carcinoma of the same stage [2,4,5]. However, collecting duct carcinoma have the worst prognosis, with a 5- year survival rate less than 5% [5]. CT imaging posing a diagnostic dilemma for the practicing physician because

it can provide detailed information about tumor itself and whether it has extended into perinephric fat or renal vein[10]. So it can play an important role in treatment planning.

II. MATERIALS AND METHODS

a) Patients

A computerized search of our institution's medical records dated between February, 2014 and February, 2016 generated a list of 64 patients who had undergone nephrectomy for renal cell carcinoma. Of these 64 patients, the diagnosis for 39 patients with a pathologic diagnosis of clear cell carcinoma and 25 patients with non-clear cell carcinoma (6 with papillary cell carcinoma, 3 with chromophobe cell carcinoma, 2 with pelvicalyceal urothelial carcinoma, 2 with pelvicalyceal urothelial papillary carcinoma, 2 with Wilms' tumor, 2 with sarcomatoid RCC, 1 with clear cell papillary carcinoma, 1 with clear cell sarcoma, 1 with malignant rhabdoid tumor, 1 with leiomyosarcoma, 1 with renal cell carcinoma associated with X11.2 dislocation TF3 fusions, 2 with angiomyolipoma and 1 with oncocytoma). 2 patients of angiomyolipoma and 1 patient of oncocytoma were excluded due to their benign characteristics. Therefore, 22 patients of non-clear cell carcinoma were included in our study. For the clear cell carcinoma (n=39; men 23, women 16; age range: 26-77 year; mean age: 54.59 +11.05 years). For non-clear cell carcinoma (n=22; men 16, women 6; age range: 0.3-74 year; mean age: 43.82 +/- 23.7 year)

b) CT examination

All patients underwent pre-operative plain CT and triphasic DCE-CT examinations using a dual-source CT scanner (Somatom Definition; Siemens, Germany) and with our standard renal mass protocol tailored to each scanner. CT images were obtained during patient breath holding with following parameters - gantry rotation time: 0.33s; tube potential: 100kV_p; effective tube current: 100mA; pitch: 1.2; collimation: 32mm x 0.6mm; beam collimation: 64mm x 0.6mm; slice thickness: 5mm and intersection gap: 5mm. All patients received oral contrast materials 30 minutes before CT. Unenhanced images were acquired before the intravenous injection of contrast media. After administering contrast agent (Ultravist, 1.5 ml/kg) with a power injector at a flow rate of 3.0ml/sec, corticomedullary, nephrographic and excretory phase images were obtained at 25-45sec, 60-90sec, 240-300 sec respectively. All images were sent to our enterprise-wide picture archiving and communications system to be interpreted on workstations.

c) Image analysis

Two experienced genitourinary radiologists who were aware that patients were being evaluated for renal lesions, but they were blinded to any other clinical, pathologic or imaging findings. Before, image interpretation, the readers met and agreed on the CT

features to be used to characterize renal masses and a data collection form. They reviewed the CT scans at picture archiving and communications system. They compared patient age, sex; size and shape of tumor; margin whether well-defined or ill-defined; location; presence or absence of calcification, hemorrhage, necrosis or any cystic change; presence or absence of thrombus in renal vein or inferior vena cava, ascites and lymphadenopathy; pattern (homogeneous or heterogeneous) and degree of enhancement (hyperdense, hypodense or isodense). For comparison of location, they described it in three patterns: Location 1 (tumor located either right or left side); Location 2 [tumor involved upper, middle, lower pole or mixed (involvement of more than one pole)]; Location 3 [involved cortex, medulla, pelvis or mixed (involvement of more than one layer)].

d) Statistical analysis

Analysis were performed by using SPSS17.1 software. We used the Pearson χ^2 test to compare the distribution of features across the two groups. A P value less than 0.05 indicated a statistically significant difference.

III. RESULTS

Of 64 renal lesions included in this study, 39 were clear cell RCCs, 25 were non-clear cell RCCs. 3 of 25 non-clear cell renal carcinoma (2-angiomyolipoma and 1-oncocytoma) were excluded as their benign behavior. So, total number of non-clear cell carcinoma were 22. Patient presented for CT examination at the CT laboratory from February, 2014 to February, 2016. The CT images were analyzed retrospectively.

Baseline characteristics for each of the groups are presented in table 2:

Table 2: Characteristic ccRCC non-ccRCC

Characteristic	ccRCC	non-ccRCC
<u>Sex</u>		
male	23	16
female	16	06
Mean age(years)	54.59+/- 11.05	43.82+/-23.7
Mean size(cm)	5.08+/-3.57	6.18 +/-2.89
Hemorrhage	03	02
Necrosis	24	18
Calcification	03	06
<u>Rim</u>		
clear	12	10
Unclear	27	12
<u>Shape</u>		
round	34	17
irregular	05	05
Homogeneous	18	03
Heterogeneous	21	19
Hyperdense	21	00
Hypodense	08	21
Isodense	10	01
<u>Location1</u>		
Right	21	13
Left	18	09
<u>Location-2</u>		
Upper	07	01
Middle	15	06
Lower	09	00
Mixed	08	15
<u>Location-3</u>		
Cortex	02	00
Medulla	33	00
Pelvis	00	02
Mixed	04	20
Metastases	04	03

There were no significant differences, when we compared age; sex; shape of tumor; presence or absence of (necrosis, hemorrhage) in between two groups.

But, when we analyzed the degree of enhancement (hyperdensity, isodensity, hypodensity) in arterial (corticomedullary) and venous (nephrographic) phases showed significant difference. In arterial phase, most of clear cell RCC (21 of 39, 53.8%) showed hyperdensity, whereas none of non-ccRCC (0 of 22,0%) showed hyperdensity. The P value was 0 ($P<0.05$). In venous phase, ccRCC showed more hyperdensity or isodensity (9 and 4 of 39, 23.1% and 10.3% respectively) than non-ccRCC (0 and 1 of 22, 0% and 4.5% respectively). Almost all of the non-clear cell RCC (21 of 22, 95.5%) showed hypodensity in both arterial and venous phases.

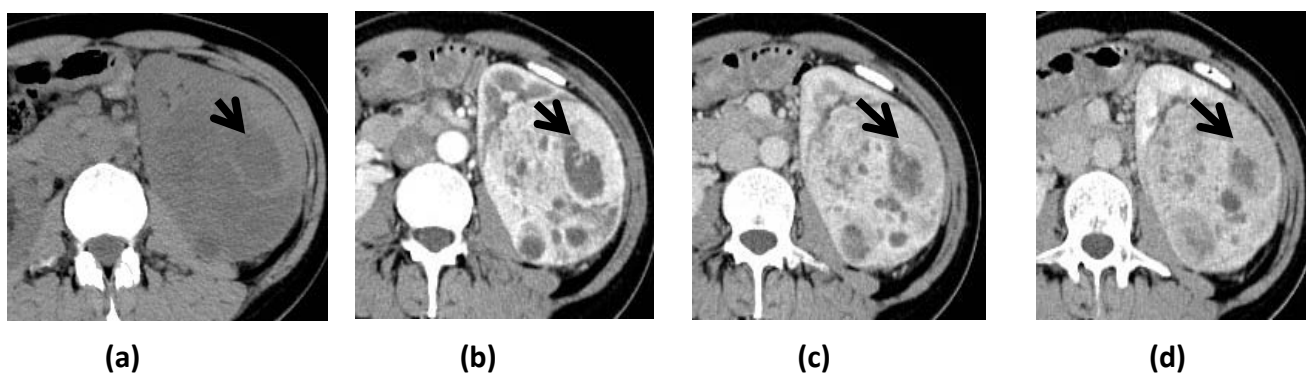


Figure 1: (a) Pre-contrast, (b) Corticomedullary, (c) Nephrographic, (d) Excretory phase-A case of clear cell renal carcinoma in a 49 years old female measuring 8 cm in diameter showing hyperdense, heterogeneous enhancement with internal necrosis (arrow).

However, we did not get any significant comparison of degree of enhancement in different difference, when compared degree of enhancement in phases in between ccRCC and non-ccRCC. delayed phase (excretory phase). Table 3: shows the

Table 3: Comparison of degree of enhancement in between ccRCC and non-ccRCC

Types	Arterial Phase			Venous Phase		
	Iso	Hypo	Hyper	Iso	Hypo	Hyper
ccRCC (n =39)	10	8	21	4	26	9
Non-ccRCC(n=22)	1	21	0	1	21	0
P value	P =0			P =0.028		
ccRCC = Clear cell renal carcinoma , non –ccRCC = Non clear cell renal carcinoma . Iso= Isodense Hypo= Hyperdense Hyper = Hyperdense						

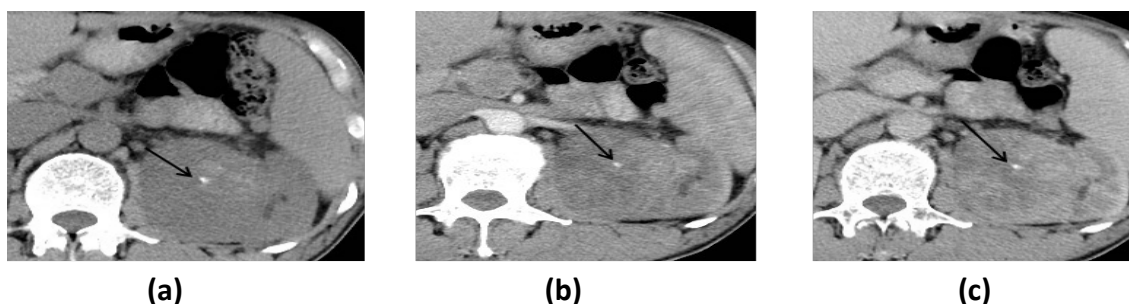


Figure 2: (a) Pre-contrast, (b) Corticomedullary phase, (c) Nephrographic phase : A case of papillary renal cell carcinoma in a 43 years old male, measuring 7cm in diameter showing calcification (arrow), necrosis and heterogeneous enhancement pattern.

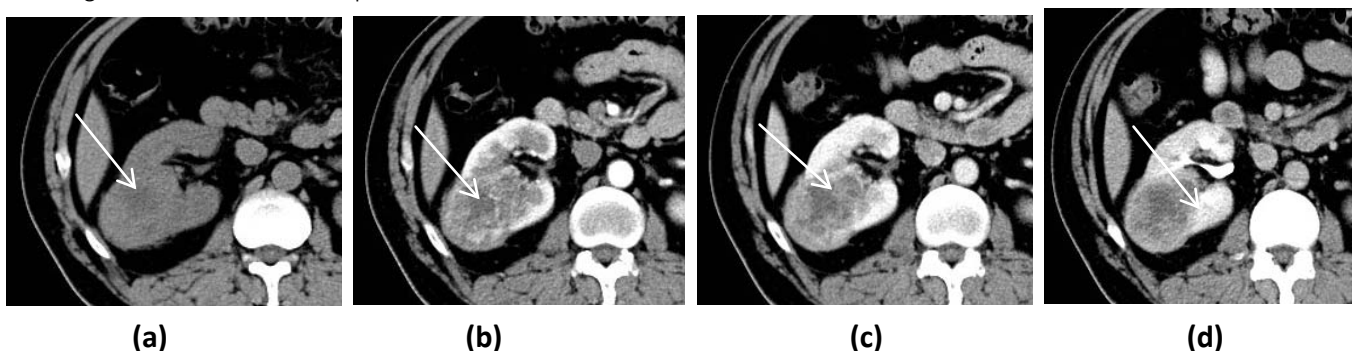


Figure 3: (a) Pre-contrast phase, (b) Corticomedullary phase, (c) Nephrographic phase, (d) Excretory phase of a case of chromophobe cell renal carcinoma in 47 years old male measuring 5.5cm in diameter showing hypovascular heterogeneous enhanced pattern with necrosis (arrow)

The pattern of enhancement (homogeneous or heterogeneous) showed significant difference. Non – clear cell carcinoma (19 of 22, 86%) showed more heterogeneous enhancement pattern than that of clear cell carcinoma (21 of 39,53%). The P value was 0.012 ($p<0.05$).

When, compared location of tumor (whether it involved upper, middle or lower pole of kidney), we found that 15 of 39 (38.5%) ccRCC were located in middle pole; but most of non-clear RCC (15 of 22,68%) did not show any specific polarity predilection. They involved two or all of 3 poles. The P value was 0.001($p<0.05$)

Most of the clear cell RCC (33 of 39,84.6%) showed involvement of medulla, whereas most of the non clear cell RCC (20 of 22,90%) did not show such predilection for a specific layer. They involved more than one layer. the P value was significant ($p=0$). But when, we compared involvement of pelvis, we found that non-ccRCC (2 of 22,9%) showed more pelvis involvement than ccRCC (0 of 39,0%).

Calcification is more common in non-clear cell RCC 27% (6 of 22) than clear cell RCC 7% (3 of 39).The p value was significant ($p=0.038$).

Table 4: Shows those parameters which have significant P value--

Types	Pattern of enhancement		Location 2				Location 3				Calcification	
	Homo	Hetero	1"	2"	3"	4"	1"	2"	3"	4"	Yes	No
ccRCC	18	21	7	15	9	8	2	33	0	4	3	36
Non-ccRCC	03	19	1	6	0	15	0	0	2	20	6	16
P value	P=0.012		P=0.001				P=0				P=0.038	
NOTE: ccRCC=Clear cell renal carcinoma ;Non-ccRCC=Non clear cell renal carcinoma ; Homo=Homogeneous ; Hetero=Heterogeneous Location 2 (1"=upper pole, 2"=middle pole, 3"=lower pole, 4" =mixed) Location 3 (1"=cortex, 2"= medulla, 3"= pelvis, 4"=mixed)												

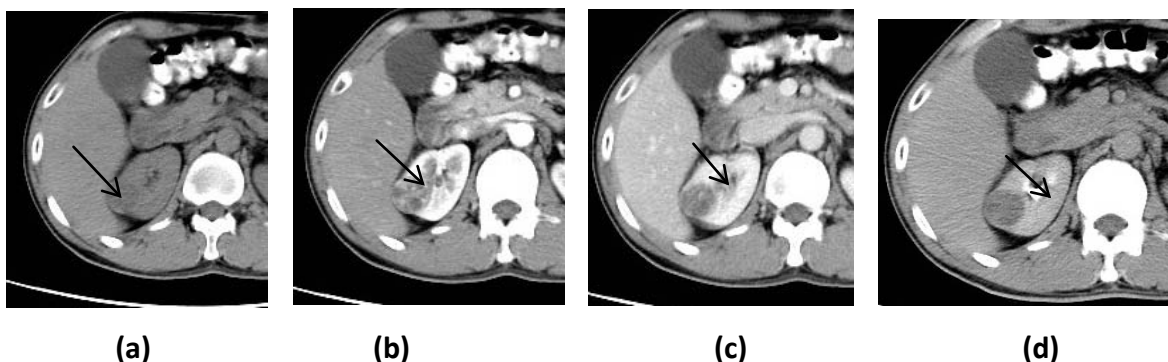


Figure 4: (a) Pre-contrast, (b) Corticomedullary, (c) Nephrographic, (d) Excretory phase -A case of clear cell renal carcinoma in a 32 years old male measuring 1 cm in diameter showing hypodensity after contrast administration.

In our study, we also made comparison in between non- clear cell RCC and clear cell RCC with hypovascular tumor. We found significant p values when we compared size, location, pattern of enhancement and presence or absence of necrosis in between these two types.

The mean size of hypovascular ccRCC was (3.92 ± 1.89) cm, whereas mean size of non-ccRCC was (6.18 ± 2.89) cm. The P value was 0.023($P<0.05$).

Non-clear cell carcinoma (19 of 22, 86.4%) showed more heterogeneous enhancement pattern than hypovascular clear cell RCC (2 of 8, 25%). P value was 0.003 ($p<0.05$).

When, we compared presence or absence of necrosis, we found that, necrosis was more common in non-clear cell RCC (18 of 22, 81.8%) than ccRCC with hypovascular tumor (2 of 8, 25%). The P value was significant ($P=0.007$).

In our study, we also found that most of non-clear cell RCC layers (20 of 22, 90.9%) showed mixed involvement of different layer of kidney (cortex, medulla and pelvis) that means no specific predilection for any layer, whereas most of hypovascular ccRCC (4 of 8, 50%) showed involvement of medulla. The p was 0 (<0.05).

Table 5: Summaries difference in between hypovascular ccRCC and non-ccRCC:

	Pattern of enhancement		Necrosis		Location 3			
	Homo	Hetero	No	Yes	1”	2”	3”	4”
Hypo ccRCC (n=8)	06	02	06	02	02	04	00	02
Non-ccRCC (n=22)	03	19	04	18	00	00	02	20
P value	P=0.003		P=0.007		P=0.00			
Note: Hypo ccRCC=Hypovascular clear cell renal carcinoma ,Non-ccRCC=Non-clear cell renal carcinoma, Homo=Homogeneous, Hetero=Heterogeneous Location 3 (1”=Cortex, 2”=Medulla, 3”=Pelvis,4”=Mixed)								

However, there were no significant differences in between hypovascular ccRCC and non-ccRCC, when we made comparison for shape (round or lobulated), rim (clear or unclear), presence or absence of (hemorrhage, calcification and metastasis). The P values were (>0.05).

IV. DISCUSSION

Now-a-days, the incidence of renal cell carcinoma is increasing due to increasing risk factors (obesity, smoking) and utilization of modern imaging techniques [11-13, 29]. A majority of renal tumors are incidentally diagnosed on medical imaging, that's why most of them are asymptomatic, small in size and present at an earlier stage [14,27]. It is important to discriminate clear cell RCC from non-clear cell RCC because of ccRCC is generally considered to have a worse prognosis and is treated differently than other subtypes [15-18,27]. Several study has been done previously to differentiate clear cell RCC from non-clear cell RCC by using imaging modalities. The most consistent finding was that, degree of enhancement was the most valuable parameter for differentiation of renal cell carcinoma subtypes. Clear cell RCCs enhance to a greater degree than other subtypes of malignant lesions [8,10,19-22]. Some researchers stated that the strong enhancement of conventional renal carcinoma is caused by its rich vascularity and alveolar architecture at histologic examination [4,10,23]. Our study consistent with these study. In this study, we found ccRCC (53.8%) showed more hyperdensity than that of non-ccRCC(0%). Most of non-ccRCC (95.5%) had hypodensity in all phases.

However, when we compared pattern of enhancement, most of clear cell RCC (53.5%) showed heterogeneity, which agree with other studies related with pattern of enhancement of ccRCC [8,10]. But, when we made comparison of heterogeneity in between ccRCC and non-ccRCC, we found that, non-ccRCC were more heterogeneous than ccRCC. This may be because of larger size of non-ccRCCs which tended to show heterogeneity due to propensity of hemorrhage,

necrosis and calcification [24-26]. At microscopic examination, all tumors with homogeneous enhancement were mainly composed of solid elements, whereas all tumors with heterogeneous enhancement had solid elements, necrosis, hemorrhage and calcifications.

When, we made comparison in between clear cell RCCs and non-clear cell RCCs for the presence of calcification, we found that calcification was significantly more in non-ccRCC (27%) than that of ccRCCs (7%). Calcification suggests a higher 5- years survival rate [3,10].

To our knowledge, it is the first study which made comparison in between two groups for the predilection of pole (upper, middle, lower) and for the involvement different layer (cortex, medulla, pelvis). We found that ccRCC showed more middle pole predilection (84%) than that of non-ccRCC (27.3%), whereas majority of non-ccRCC showed mixed polarity means involvement of more than one pole (68.2%). ccRCC (84.6%) had predilection for involvement of medulla, whereas most of the non-ccRCC (90%) had no specific predilection for any layer, they involved more than one layer. In case of pelvis involvement, non-ccRCC (9%) showed more pelvis involvement than that of ccRCC (0%).

In this study, we also made comparison in between ccRCC which showed hypovascularity and non-ccRCC. The number of ccRCC with hypovascularity was 8. Non-ccRCC (86.4%) were more heterogeneous than hypovascular ccRCC (25%). We also found that, necrosis was more common in non-ccRCC (81.8%) than hypovascular ccRCC (25%) and involvement of pelvis was more common in non-ccRCC (9.15%) than hypovascular ccRCC (0%). Hypovascular ccRCC (50%) showed predilection for involvement of medulla and most of non-ccRCC (90.9%) did not show any specific predilection for involvement of cortex, medulla and pelvis, rather than they showed involvement of more than one layer (mixed involvement).

Our study had few potential limitations. First, our study was retrospective study. Second, we did not measure CT value of different kinds of tumor. Third, we

did not compare clear cell renal carcinoma with any other specific type of non-clear cell renal carcinoma. We compared ccRCC with as a whole others non-ccRCC. So, it may be a limitation. The study population of non-clear cell renal carcinoma was small in number.

Disclosures:

The authors indicated no financial relationships.

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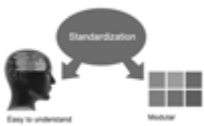
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