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Magnetic Resonance Spectroscopic Imaging (MRSI) Study of Breast Cancer

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ABSTRACT

Background: Breast cancer is the fifth most common cause of cancer death worldwide and most serious form of neoplastic diseases in both developed and developing countries. Mammography and ultrasound are the most often used screening methods in breast cancer. Magnetic Resonance Imaging (MRI) uses the protons in water and fat to create the image of breast cancer. But recent studies says neoplastic breast lesions contains elevated choline concentration (tCho) and altered mean apparent diffusion coefficient (ADC) which can be used as good biomarkers to evaluate the cancer stages even follow up the Neoadjuvent Chemotherapy (NACT).

Aim & Objectives:

- 1. To evaluate the relation of age, tCho concentration and mean ADC with breast cancer.
- 2. To estimate the correlation between the factors.
- 3. To calculate the main difference between breast cancer patient before and after menopause.

Methods/Study Design: This was a cross sectional, observational study done on 14 randomly selected diagnosed stage I breast cancer patients newly registered in surgery department of All India Institute of Medical Sciences, New Delhi, India during 3 months study period. Intentionally 7 of them were selected to be postmenopausal and rest 7 premenopausal. Patients with claustrophobia, serious illness, pacemaker or associated diseases were excluded. Volunteers were selected by lottery method after confirmation of absence of the exclusion criteria in them. All the breast MRS images were taken only after signing the consent form of being a volunteer for the study with breast coil. All the spectroscopic images were analyzed with computer technologies and SPPS software with the help of non-parametric statistical tests.

Results/Findings: Mean age of patients were 44.85 ± 6.97 where in premenopausal and postmenopausal women it was 40.14 ± 4.59 and 49.57 ± 5.26 respectively. tCho concentration was high in postmenopausal women (4.85 ± 2.64 mmol/kg vs 3.72 ± 1.64) where unlike to them premenopausal women showed higher mean ADC values (1.02 ± 0.20 vs 0.91 ± 0.09). All together weak correlation (r= 0.439) found in between the tCho and mean ADC where age and tCho were weakly correlated among the premenopausal patients (r=0.440). Among the postmenopausal women strong correlation found in between age tCho and mean ADC (r=0.620) and age and mean ADC (r=0.498).

Study Limitations: It was short term study with very less population of same category of breast cancer which can be more appreciated if done in a large population cohort study design though as a pilot study the aims were satisfactorily reached.

Conclusion: Postmenopausal women show adverse conditions in breast cancer and using tCho and mean ADC as biomarkers; the management process becomes easier for a doctor.

Keywords: Breast Cancer, MRSI, MRI, Cancer Biomarkers

Background

Breast cancer is one of the most prevalent and serious forms of neoplastic disease affecting women in both developing and developed countries and is a significant cause of morbidity and mortality. Worldwide it is the fifth most common cause of cancer death. In 2005. breast cancer caused 502.000 deaths which constituted 7% of all cancer deaths and almost 1% of total deaths.¹ In India it is the second leading cause of cancer related deaths among women first being the cervical cancer.² In the two major cities, Delhi and Mumbai the incidence of breast cancer is now rapidly catching up with the cervical cancer. Infact, one out of every 20 women in Delhi and Mumbai has been reported to have the risk of developing the breast cancer in these cities.³ The age-standardized rate of breast cancer has been documented as 22 to 28 per 100000 women per year in India.⁴ Although the rates appear to be lower than those seen in developed countries, the burden of cancer in India is alarming.

Breast cancer develops in ducts and lobules. It can also develop in males but occurrence is rare. Genetic studies on heredity of breast cancer indicated that mutations in BRCA1 and BRCA2 were present in approximately 45% 35% and of breast cancer patients respectively.^{5,6} Carriers of BRCA1 and BRCA2, are also at a very high risk of developing breast cancer in their lifetime. Additionally the risk of recurrence is 50% higher in them by 70 years of age.⁷

Till date there is no single method for diagnosis and treatment management of breast cancer or which can completely cure the disease. The primary strategy therefore is to reduce the mortality in early detection and treatment. Mammographies, Ultrasound, Cytological assessment with Fine Needle Aspiration Cytology (FNAC) etc are having a role to diagnose breast CA and to help in management though improper and having errors.⁸⁻¹⁶

Magnetic Resonance Imaging (MRI) uses the protons in water and fat to create the image of breast cancer. But recent studies says neoplastic breast lesions contains elevated choline concentration (tCho) and altered mean apparent diffusion coefficient (ADC) which can be used as good biomarkers to evaluate the cancer stages even follow up the Neoadjuvent Chemotherapy (NACT).

Aim & Objectives

- 1. To evaluate the relation of age, tCho concentration and mean ADC with breast cancer.
- 2. To estimate the correlation between the factors.
- 3. To calculate the main difference between breast cancer patient before and after menopause.

Methods / Study Design

- <u>Study design:</u> It was a cross sectional, observational descriptive study
- <u>Study area:</u> All India Institute of Medical Sciences, New Delhi

• <u>Study period:</u> 3 months

- 14 Study population: randomly selected volunteer who are diagnosed as stage I breast cancer patients newly registered in surgery department of All India Institute of Medical Sciences, New Delhi were taken as study population as well sample. as Intentionally 7 of them were selected to be postmenopausal and rest 7 premenopausal to fulfill the aim.
- <u>Exclusion criteria:</u> Patients with claustrophobia, serious illness, pacemaker or associated diseases were excluded from the study.

Tools

- 1. Informed consent form
- 2. MRI machine with all necessary instruments with it. (Siemens Magneto Sonata/Avanto, Erlangen, Germany)
- 3. Computer with statistical software

Methodology

<u>Ethical Safeguard:</u> Necessary permission from Institutional Ethical Committee were taken as ethical committee clearance. All the participants are requested to volunteered for the study only after filling up and signing the detailed informed consent form which was written in their own local language i.e. Hindi. Illiterate participants were requested to come along with a literate family member or friend to do the job on behalf of them.

<u>Imaging and Spectroscopy:</u> MRI/MRS was carried out on a standard clinical 1.5T whole body MR scanner (Siemens Magneto Sonata/Avanto, Erlangen, Germany) at the Department of N.M.R., AIIMS. The subjects were positioned prone and the breasts were immobilized using foam-pads, in a dedicated double breast coil (circularly polarized, phased array).

MRS uses MR images for localisation of voxel from which spectroscopy were acquired. All patients were imaged according to standard protocol. Following the scout image, either T₁ or T₂ weighted images in saggital plane were obtained using a standard pulse sequence. Fat suppressed images in axial and coronal planes were acquired to identify the full extent of irregular border of the tumor. DCE-MRI was carried out using a fatsaturated 3DFLASH sequence whenever required for proper identification of the tumour. The in-vivo proton MRS was carried out using STEAM/PRESS pulse sequence prior to spectral acquisition; magnetic field shimming was performed over the voxel region for getting maximum magnetic field homogeneities. Sixty-four to one hundred and twenty eight scans were collected with simultaneous water and lipid suppressed pulse sequence (TR=2000 ms, TE=30 or 135 to 270 ms) in order to improve the detection of present metabolites in millimolar concentration. 2D¹H-MRSI was performed using PRESS sequence (TR=2000 ms, TE=30-270 ms) on a 10-20 mm thick slab placed on the tumor using T₂-weighted image as scout. The voxel volume would range from 0.8 to 1 cm^3 .

<u>Data compilation/collection:</u> All clinical, MR image and spectroscopic data were compiled using statistical software in computer.

<u>Statistical analysis:</u> Keeping in view of specific objectives of the study and distribution of generated data, the appropriate bio-statistic methods were applied for the data analysis to the MRS, clinical data. The results were considered significant at 5% level of significance. SPSS and MS Excel were used

to statistically analyze the data with non-parametric tests.

<u>Report Writing:</u> With all data and statistical values in hand report was written in scientific way with wide range of information for reader in a short space and was submitted to authority concern.

Results or Findings

All the results are shown in tables bellow and followed by main findings with little explanations.

Mean age of all patients were 44.85 ± 6.97 where in premenopausal and postmenopausal women it was 40.14 ± 4.59 and 49.57 ± 5.26 respectively. tCho concentration was high in postmenopausal women (4.85 ± 2.64 mmol/kg vs 3.72 ± 1.64) where unlike to them premenopausal women showed higher mean ADC values (1.02 ± 0.20 vs 0.91 ± 0.09).

All together weak correlation (r= 0.439) found in between the tCho and mean ADC where age and tCho were weakly correlated among the premenopausal patients (r=0.440). Among the postmenopausal women strong correlation found in between age tCho and mean ADC (r=0.620) and age and mean ADC (r=0.498).

Study Limitations

- 1. It was short term study
- 2. Very less population of same category of breast cancer which can be more appreciated if done in a large population cohort study design

-though as a pilot study the aims were satisfactorily reached.

Conclusion

Postmenopausal women show adverse conditions in breast cancer and using tCho and mean ADC as biomarkers; the management process becomes easier for a doctor.

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Serial no.	Age	Menopausal Status	tCho	Mean ADC
1	50	Post	10.81512	0.784
2	53	Post	3.35	1.018
3	39	Pre	6.462693	1.028
4	47	Post	4.308	0.752
5	32	Pre	1.76	0.912
6	52	Post	3.87	1.006
7	46	Pre	3.34	1.249
8	40	Pre	3.27	0.87
9	58	Post	1.85	0.96
10	39	Pre	2.338879	1.268
11	40	Post	5.58	0.861
12	45	Pre	5.310839	0.713
13	47	Post	4.2	0.94
14	40	pre	3.6	1.0837
Mean value	44.85714		4.289681	0.960336
SD	6.970897		2.314715	0.166328

Table 1: Frequency distribution table showing the mean values of Age, tCho and Mean ADC

Table 2: Frequency distribution table showing the correlation between Age, tCho and Mean ADC among all participants

Serial No	tCho	mean ADC	Age	tCho	Age	mean ADC
1	10.81512	0.784	50	10.81512	50	0.784
2	3.35	1.018	53	3.35	53	1.018
3	6.462693	1.028	39	6.462693	39	1.028
4	4.308	0.752	47	4.308	47	0.752
5	1.76	0.912	32	1.76	32	0.912
6	3.87	1.006	52	3.87	52	1.006
7	3.34	1.249	46	3.34	46	1.249
8	3.27	0.87	40	3.27	40	0.87
9	1.85	0.96	58	1.85	58	0.96
10	2.338879	1.268	39	2.338879	39	1.268
11	5.58	0.861	40	5.58	40	0.861
12	5.310839	0.713	45	5.310839	45	0.713
13	4.2	0.94	47	4.2	47	0.94
14	3.6	1.0837	40	3.6	40	1.0837
Mean	4.289681	0.960336	44.85714	4.289681	44.85714	0.960336
SD	2.314715	0.166328	6.970897	2.314715	6.970897	0.166328
Correlations	$r^2 = 0$	0.193	$r^2 = 0$	0.012	$r^2 = 0$	0.153
(r)	r= 0.439		r= 0.109		r= 0.391	

Serial No	tCho	mean ADC	Age	tCho	Age	mean ADC
1	6.462693	1.028	39	6.462693	39	1.028
2	1.76	0.912	32	1.76	32	0.912
3	3.34	1.249	46	3.34	46	1.249
4	3.27	0.87	40	3.27	40	0.87
5	2.338879	1.268	39	2.338879	39	1.268
6	5.310839	0.713	45	5.310839	45	0.713
7	3.6	1.0837	40	3.6	40	1.0837
Mean	3.726059	1.017671429	40.14286	3.726059	40.14286	1.017671
SD	1.641304	0.202666283	4.598136	1.641304	4.598136	0.202666
Correlations	$r^2 = 0.046$		$r^2 = 0.194$		$r^2 = 0.006$	
(r)	r= 0.2144		r= 0.44045		r= 0.07745	

Table 3: Frequency distribution table showing the correlation between Age, tCho and Mean ADC among premenopausal women

Table 4: Frequency distribution table showing the correlation between Age, tCho and Mean ADC among postmenopausal women

Serial No	tCho	mean ADC	Age	tCho	Age	mean ADC
1	10.81512	0.784	50	10.81512	50	0.784
2	3.35	1.018	53	3.35	53	1.018
3	4.308	0.752	47	4.308	47	0.752
4	3.87	1.006	52	3.87	52	1.006
5	1.85	0.96	58	1.85	58	0.96
6	5.58	0.861	40	5.58	40	0.861
7	4.2	0.94	47	4.2	47	0.94
Mean	4.853303	0.903	49.57143	4.853303	49.57143	0.903
SD	2.646889	0.097964	5.260558	2.646889	5.260558	0.097964
Correlations	$r^2 =$	0.385	$r^2 = 0$	0.122	$r^2 =$	0.24
(r)	r= 0.6204		r= 0.349		r=0.48989	