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"Diagnostic accuracy of AMACR in differentiating the prostate malignancy from benign and its mimickers"

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ABSTRACT

Background: The diagnosis of prostate cancer (PC) is based on a mix of architectural, cytological, and ancillary aspects, none of which is completely sensitive and specific. Present study aimed to study the AMACR in differentiating the prostate malignancy from benign and its mimickers.

Material & Method: The present cross-sectional study was conducted among 40 cases for period of 2years from Nov 2016 to May 2018 at department of Pathology, Bangalore Medical College, Bengaluru. It included the include 40 prostate biopsies/transurethral resection of prostate (TURP) specimens/prostatectomies received from the Department of Urology. All the specimens obtained were fixed in buffered neutral formalin and stained for H& E and histopathological evaluation, AMACR cellular localisation, as granular and cytoplasmic, positive control is of prostate cancer.

Result: Total of 40 prostate samples, with 13 cases showing benign and malignant lesions and 14 cases with premalignant lesions. AMACR showed 100% sensitive in malignant cases and specificity of AMACR is 14.29% in differentiating malignant and premalignant cases. AMACR is 100% sensitive and specific in differentiating benign and malignant prostatic lesions.

Conclusion: Concluded that AMACR is of great value in differentiating HGPIN and malignant glands from benign glands.

Keywords: Prostate, Carcinoma, Malignant, AMACR, Histopathology.

Introduction:

Prostate cancer is usually seen in adults more than 50yrs of age. It increases from 20% in their 50s to approximately 70% in between the ages of 70 and 80 years. Adenocarcinoma of prostate is the most common form of cancer in men, accounting for 29% of cancer in the united states in 2012.(1) The incidence rates of prostate cancer differ from place to place from a low of 6.3 to a high of 83.4 per 100,000 men.(2) The incidence rate of prostate cancer in India is predicted to be 9 per 100,000 males, 12.4 in Delhi, and 5.86 in the Pune Metropolitan Region.(3–5) Prostate cancer incidence rates in North East India are modest, with three cases per 100,000 males in Mizoram, 1.6 in Meghalaya, 1.5 in Manipur, and one in Tripura.(4)

The diagnosis of prostate cancer (PC) is based on a mix of architectural, cytological, and ancillary aspects, none of which is completely sensitive and specific. Accurate tissue diagnosis can be very challenging due to the presence of either a small focus of cancer or due to the presence of many benign mimickers of malignancy like sclerosing adenosis, partial atrophy, adenosis, atrophy, clear cell cribriform hyperplasia, nephrogenic adenoma, basal cell hyperplasia, post atrophic hyperplasia, radiation atypia, mesonephric hyperplasia, seminal vesicle and cowpers glands.(6)

Because of the widespread use of blood PSA (Prostate Specific Antigen) as a mass screening test for prostate cancer, the number of prostate needle biopsies has increased, as has the requirement to provide an accurate diagnosis despite the restrictions. On final radical Prostatectomy, 40-50% of individuals with minimal disease had moderately progressed or advanced carcinoma.(6) More recently a positive marker for prostate carcinoma, α-methyl acyl CoA racemase (AMACR) has been reported to have sensitivity ranging from 82-100%.(6) Hence, present study aimed to study the AMACR in differentiating the prostate malignancy form benign and its mimickers.

Material & Method:

The present cross-sectional study was conducted among 40 cases for period of 2years from Nov 2016 to May 2018 at department of Pathology, Bangalore Medical College, Bengaluru. It

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included the include 40 prostate biopsies/transurethral resection of prostate (TURP) specimens/prostatectomies received from the Department of Urology, Bangalore Medical College.

Procedure: All the specimens obtained were fixed in buffered neutral formalin for a period of 12-24 hrs and then the entire specimen was submitted for processing. For grossing, The weight of the specimen was noted and the findings were recorded as per the format. The entire bits were submitted for processing. Which included the steps as dehydration, clearing by chloroform, paraffin impregnation, embedded in paraffin wax, sections were cut by microtome setting of 4 microns, sections were floated in 60degree temperature, mounted on slide and for immunohistochemical analysis sections were mounted on poly-L-Lysine coated slides. The staining for light microscopy done with routine H&E to arrive at diagnosis. The AMACR cellular localisation, as granular and cytoplasmic, positive control is of prostate cancer.

Statistical analysis: all the data were analysed using SPSS 21.0 operating on windows 10. The results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Result:

A total of 40 prostate samples included in present study. Twenty-four (60%) were TURP and sixteen (40%) were core biopsy specimens. The cases were distributed in the age group of 40–95 years. The majority of cases were in the age group of 70-80yrs.

Out of forty cases, thirteen were BPH. Age group 51-60 showed, four cases of BPH. PSA was raised in four cases of BPH. Rest all the cases of BPH showed normal PSA for the given age. AMACR: In all the thirteen cases of BPH, the glands were negative for AMACR stain.

Out of forty cases, nine were high grade intraepithelial neoplasia (HGPIN). Four of Core biopsy and 5 TURP specimen showed features of HGPIN. HGPIN was observed in the age group 40-83. Out of nine cases, six cases showed raised PSA for the given age. For AMACR Out of nine cases, one case showed moderate cytoplasmic granular positivity (2+), rest of the cases showed mild cytoplasmic granular positivity (1+).

Table 1: Showing demographic details and histopathology report of all patients

		Frequency	Percent
Age	<40	1	2.5
	51-60	6	15.0
	61-70	11	27.5
	71-80	17	42.5
	81-90	4	10.0
	>90	1	2.5
Type	Core biopsy	16	40
	TURP	24	60
HPR	Atypical adenomatous hyperplasia	2	5
	Atypical small acinar proliferation	3	7.5
	Benign prostatic hyperplasia	13	32.5
	High grade prostatic intraepithelial neoplasia	9	22.5
	Prostatic adenocarcinoma	13	32.5
HPR	Benign	13	32.5
	Malignant	13	32.5
	Premalignant	14	35

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Table 2: Distribution of AMACR findings with histopathological report					
	AMACR				Total
HPR	Negative	Mild	Moderate	Strong	
Benign	13	0	0	0	13
	100.0%	0.0%	0.0%	0.0%	100.0%
Premalignant	1	9	4	0	14
	7.14%	64.2%	28.5%	0%	100.0%
Malignant	0	0	1	12	13
	0%	0%	7.69%	92.3%	100.0%
Total	14	9	5	12	40
	35%	22.5%	12.5%	30%	100.0%

Table 3: Comparison of the AMACR diagnosis with PSA of the patients					
HPR			Age specific PSA		Total
			Normal	Abnormal	
Malignant	**Benign AMACR**	Negative	10	3	13
			76.9%	23.07%	100.0%
	Total		10	3	13
			76.9%	23.07%	100.0%
		2+; moderate	0	1	1
			0%	100.0%	100.0%
		Strong	0	12	12
			0.0%	100.0%	100.0%
	Total		0	13	13
			0%	100%	100.0%
Premalignant	**AMACR**	1+, mild	3	6	9
			33.3%	66.6%	100.0%
		2+, moderate	0	4	4
			0.0%	100.0%	100.0%
		3+, strong	0	0	0
			0.0%	0.0%	0.0%
		Negative	1	0	1
			100.0%	0.0%	100.0%
	Total		1	4	5
			20.0%	80.0%	100.0%

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Table 4: Diagnostic accuracy of AMACR to differentiate malignant lesions of prostate			
		HPR	
		Malignant	Pre-malignant
AMACR	Positive	13	12
	Negative	0	2
		Percent	95% CI
Diagnostic characteristics of AMACR	Sensitivity	100%	(77.19 – 100)
	Specificity	14.29%	(4.009 – 39.94)
	Positive predictive value	52%	(33.5 – 69.97)
	Negative predictive value	100%	(34.24 – 100)
	Diagnostic accuracy	55.56%	(37.31 – 72.41)

		HPR	
		Malignant	Benign
AMACR	Positive	13	0
	Negative	0	13
		Percent	95% CI
Diagnostic characteristics of AMACR	Sensitivity	100%	(77.19 – 100)
	Specificity	100%	(77.19 – 100)
	Positive predictive value	100%	(77.19 – 100)
	Negative predictive value	100%	(77.19 – 100)
	Diagnostic accuracy	100%	(77.19 – 100)

AMACR is 100% sensitive in malignant cases. Specificity of AMACR is 14.29% in differentiating malignant and premalignant cases. AMACR is 100% sensitive and specific in differentiating benign and malignant prostatic lesions.

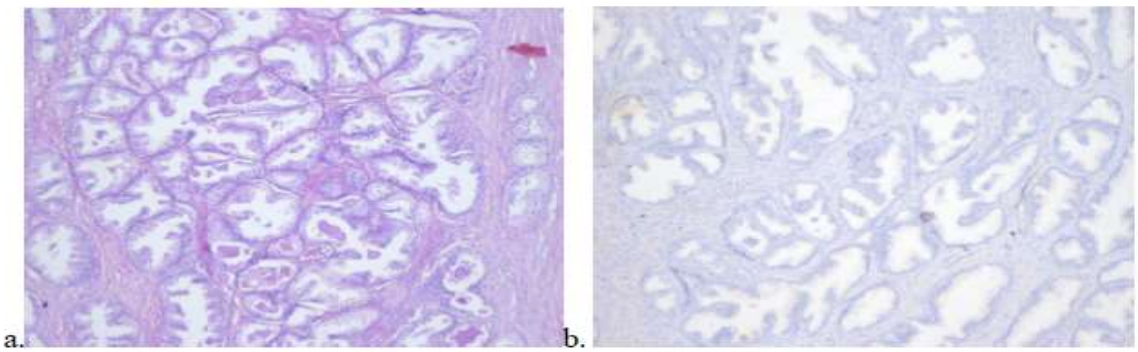

Figure 1: a. Photomicrograph of histology of BPH; b. AMACR negative stain in BPH

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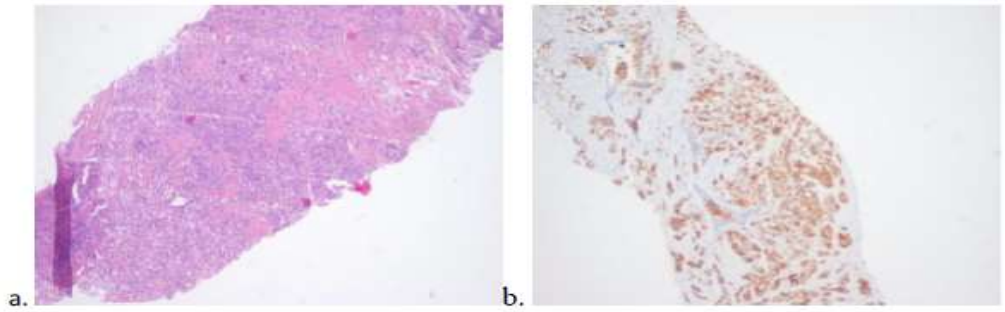

Figure 2: a. Photomicrograph of histology of adenocarcinoma of prostate; b. AMACR showing strong positivity for tumor cells in prostatic adenocarcinoma

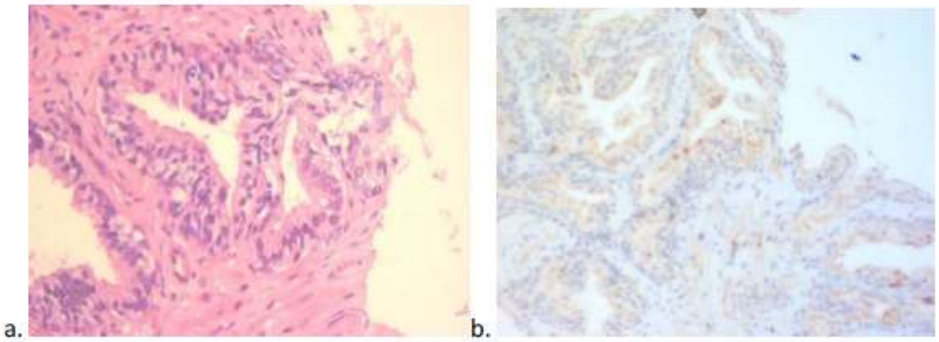

Figure 3: a. Photomicrograph of histology of HGPIN; b. AMACR showing mild positivity in HGPIN

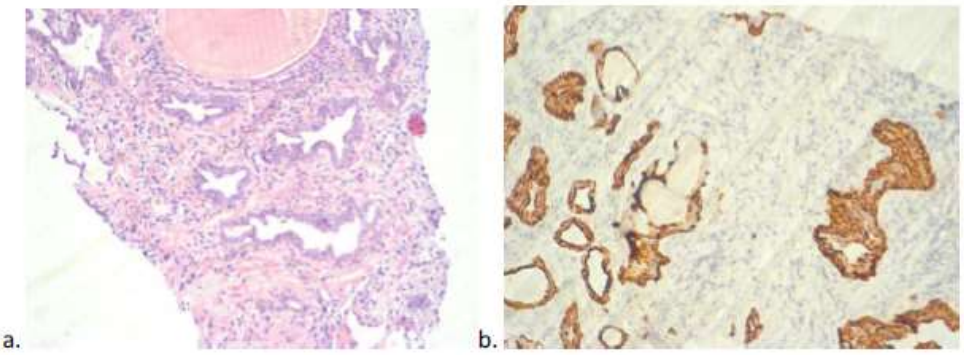

Figure 4: a. Photomicrograph of histology of ASAP; b. AMACR showing strong positivity in ASAP

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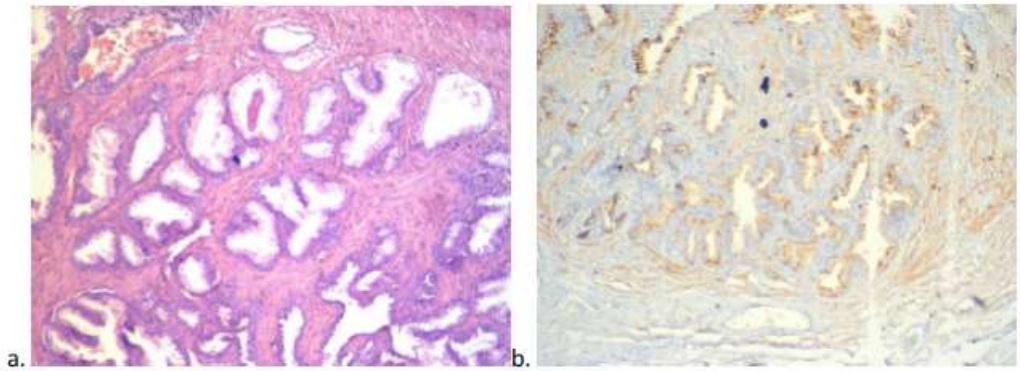

Figure 5: a. Photomicrograph of histology of FAAH; b. AMACR showing moderate positivity in FAAH

Discussion:

The diagnosis of prostate cancer (PC) is based on a mix of architectural, cytological, and ancillary aspects, none of which is completely sensitive and specific. Accurate tissue diagnosis can be difficult due to the presence of either a tiny focus of cancer or a large number of benign mimickers of malignancy.(6)

Because of the widespread use of blood PSA (Prostate Specific Antigen) as a mass screening test for prostate cancer, the number of prostate needle biopsies has increased, as has the requirement to provide an accurate diagnosis despite the restrictions. On final radical Prostatectomy, 40-50% of individuals with minimal disease had moderately progressed or advanced carcinoma.(6)

In present study, out of forty cases, thirteen were BPH, three were atypical small acinar proliferation, two were atypical adenomatous hyperplasia, nine were high grade intraepithelial neoplasia, thirteen were prostatic adenocarcinoma. IHC was done using AMACR markers in the all this cases. In our study BPH was seen in the age group of 55-85yrs of age. In a study done by M Koteshwari et al, 90.7% showed the BPH cases.(7)

In our study of 13 cases of BPH, the glands were negative for the AMACR immunostaining. The percentage of negativity was 100%. It is comparable with other studies by Kumarseran K et al.,(6) Bai EL et al.,(8) and Jain D et al.(9)

The diagnostic characteristics to differentiate the malignant from benign condition was found to be 100% sensitive and specific. Similar to present study other study by Deepika Jain et al.,(9) documented 89.1%, and 100% diagnostic accuracy was noted by other authors Lakshmi Bai et al.,(10) Molinie et al.,(11) and Yu et al.(12)

Conclusion: Using AMACR/P504S as a positive marker will enhance the diagnostic accuracy in prostate cancer and reduce the chance of misdiagnosis. Also, AMACR is of great value in differentiating HGPIN and malignant glands from benign glands.

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Conflict of interest: Nil

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