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CROSS-SECTIONAL RESEARCH ON ALPHA METHYLACYL-COA RACEMASE (AMACR) AS A DIAGNOSTIC MARKER OF CARCINOMA PROSTATE PATIENTS

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Abstract:
Objective: *Frequency determination of the positive expression of the diagnostic marker (alpha methyl acyl-COARACEMES (AMACR)) through prostate needle biopsy specimen's evaluation in the adenocarcinoma prostate patients was the objective of this research.*
Study design: *Cross-sectional study.*
Place and Duration of Study: *Research was carried out at Nishtar Hospital, Multan (Histopathology Dept), in the timeframe of April, 2016 to October, 2017.*
Material and Methods: *We diagnosed every specimen of adenocarcinoma prostate in the said setting on the grounds of routine histopathology and immunohistochemistry without any discrimination of age, histological tumor grade or type. We also calculated SD and Mean values for variables which were quantitative and for qualitative variables frequencies of age for expression of AMACR.*
Results: *Research samples comprised of eighty patients among which 68 AMACR positive cases (85%); whereas, 12 cases were negative (15%). Nine negative cases presented 1 ± staining which was weak and non-circumferential (11.3%) and zero staining was observed in three cases which were No cytoplasmic staining (3.8%).*
Conclusion*: Positive AMACR staining may be used for the cancer diagnostic through prostate needle core biopsies in the focus of under one-millimeter dimension (taken as maximum). AMACR expression outcomes in this population can be compared with the outcomes of Western research studies. Staining of AMACR need an interpretation in the perspective of basic hematoxylin context and criteria of eosin for malignancy including the outcomes of the related supportive markers expressions which includes a basal cell specified indicator such as 34βE12 or p63.*
Keywords: *Adenocarcinoma prostate, Alpha methyl acyl-CoA racemase (AMACR) and Immunohistochemistry.*

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INTRODUCTION:

Over the world the second most repeated cancer is prostate cancer specific to male population, as per the estimates 900,000 cases are reported and among these cases the death toll is observed as 258,000 (2008) [1]. Males face this malignancy as the 3rd repeated malignancy as seven percent of the cases of neoplasm malignancy are males [2]. The most important is the timely diagnosis for an early management of the cancer as in 40 – 50 percent of the cancer patients who had a limited cancer which was of advance or moderate carcinoma on the final radical prostatectomy [3]. Therefore, the treatment can be delayed because of an underdiagnosis of the limited prostatic adenocarcinoma focus and patients can experience severe consequences. Prostatic cancer diagnosis is a combination of cytological, architectural and ancillary manifestations. The challenging part is an accurate diagnosis of the tissue as there is presentation of either cancer's small focus or because of the presentation of numerous benign malignancy mimickers such as adenosis. Although basal cell's immunohistochemical stains, including high molecular weight cyto-keratin or currently p63 can be helpful in the focal prostate cancer diagnosis with few restrictions in the utilization. Basal cell marker's negative staining is an automatic carcinoma diagnostic tool. A positive marker of immunohistochemical which is also specific for the prostate cancer is of great importance, it enhances the level of confidence which is mandatory for the definitive diagnosis of the malignancy [6]. Alpha methyl acyl-COA racemase (AMACR) is also referred as (p504s), which is a cytoplasmic enzyme expressed by CDNA microarray which is also overexpressed in number of adenocarcinomas of prostate and in higher prostatic intraepithelial neoplasia, but in other words it is very weak to be expressed in the benign glands. No doubt AMACR is a very useful indicator of the prostate adenocarcinoma as stated in Western countries, in the setting of our country its effective is still is under debate. In the recent research works AMACR specificity and sensitivity for prostate adenocarcinoma diagnosis and Japanese patient's benign glands are less as reported in the past work than the Western countries [7]. Frequency determination of the positive expression of the diagnostic marker (alpha methyl acyl-COARACEMES (AMACR)) through prostate needle biopsy specimen's evaluation in the adenocarcinoma prostate patients was the objective of this research.

MATERIALS AND METHODS:

In this cross-sectional research which was carried out at Nishtar Hospital, Multan (Histopathology Dept), in the timeframe of April, 2016 to October, 2017: we diagnosed every specimen of adenocarcinoma prostate in the said setting on the grounds of routine histopathology and immunohistochemistry without any discrimination of age, histological tumor grade or type. We also calculated SD and Mean values for variables which were quantitative and for qualitative variables frequencies of age for expression of AMACR. Research was completed on eighty cases as sample population calculated through WHO calculator by keeping (APP "anticipated population proportion" as 70.66, CI as 95% and absolute precision as 10%). We took permission from the ethical committee and informed consent from the participants. Sample was selected through consecutive non-probability technique of sample selection. We did not include all the inadequate cases. Every participant was observed with histopathological diagnosis and age. SPSS software was used for data analysis and outcomes were verified by a consultant without any biasness, a single consultant verified all the outcomes. We did not score any AMACR cytoplasmic staining as zero and negative interpretation was also ignored; whereas, a weaker and non-circumferential staining was taken as 1and negative interpretation was made. Similarly, stronger circumferential staining was graded as 2 and positive interpretation was made. Age was also calculated for the descriptive statistics.

RESULTS:

Research samples comprised of eighty patients among which 68 AMACR positive cases (85%); whereas, 12 cases were negative (15%). Nine negative cases presented 1 ± staining which was weak and non-circumferential (11.3%) and zero staining was observed in three cases which were No cytoplasmic staining (3.8%) (Table – III). Table – I reflects the age wise distribution. Patients were observed with a mean age factor as (66.16 ± 8.44) years in the age bracket of (55 – 83) years. Majority of the patients were in the sixth and seventh decade and next most repeated decade was observed as fifth and eighth decade as shown in Table – I.

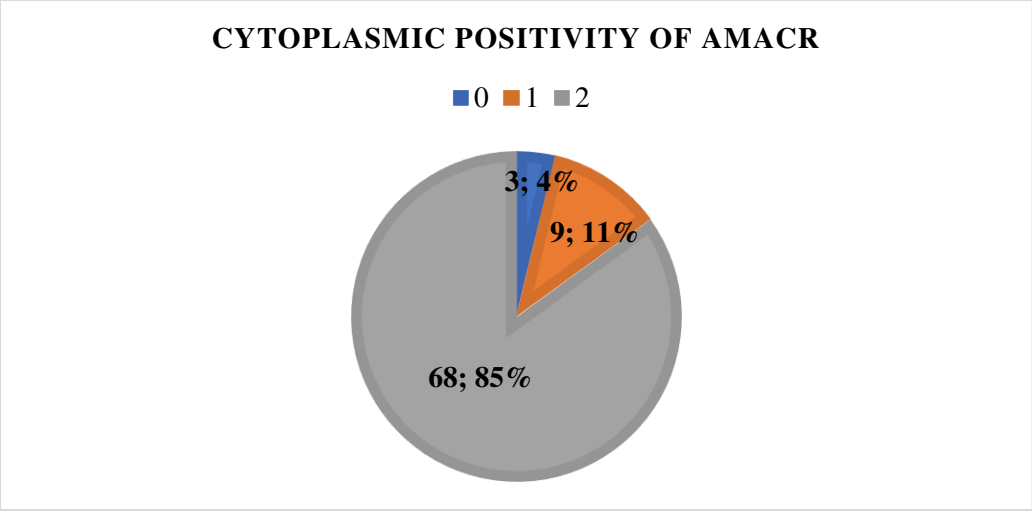


Figure – I: AMACR Cytoplasmic positivity.

For age we considered a significant P-value as (0.269).

DISCUSSION:

Over the world the second most repeated cancer is prostate cancer specific to male population, as per the estimates 900,000 cases are reported and among these cases the death toll is observed as 258,000 (2008) [1]. Males face this malignancy as the 3rd repeated malignancy as seven percent of the cases of neoplasm malignancy are males, subcontinent reports the same incidences as reported worldwide. [2]. The prostate cancer risk in a complete life span of male in the USA is reported with an approximation of one case among six cases [2].

Table – I: Age and intensity of AMACR staining score

Intensity Score	Age			Total
	50-60	61-70	71-85	
0	0	2	1	3
1	2	2	5	9
2	23	28	17	68
Frequency	25	32	23	80
Percentage	31.2	40	28.8	100

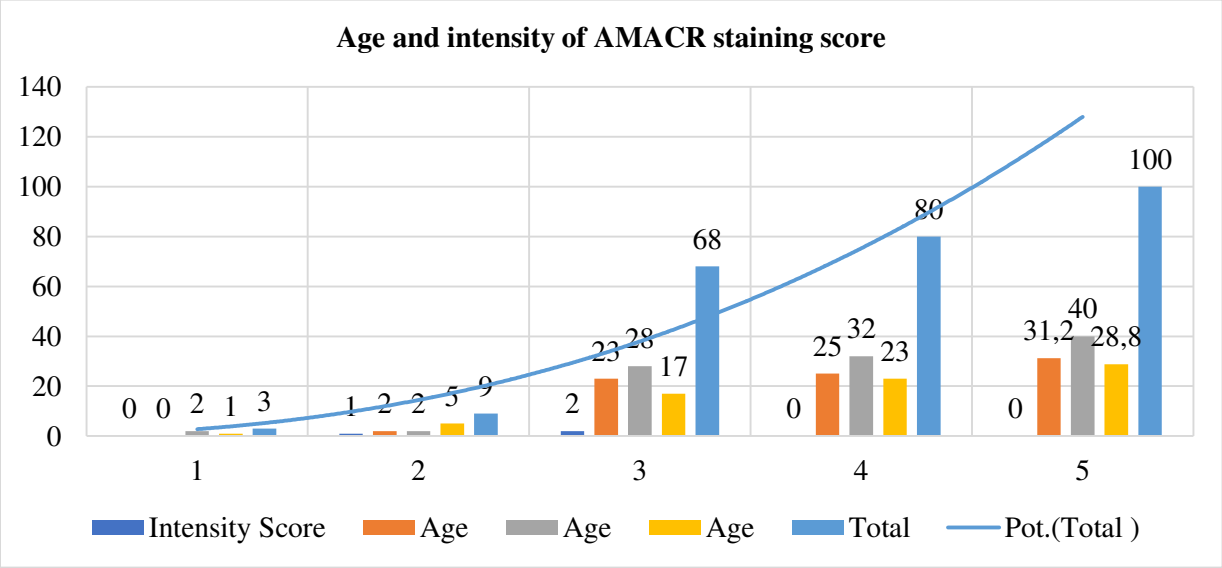
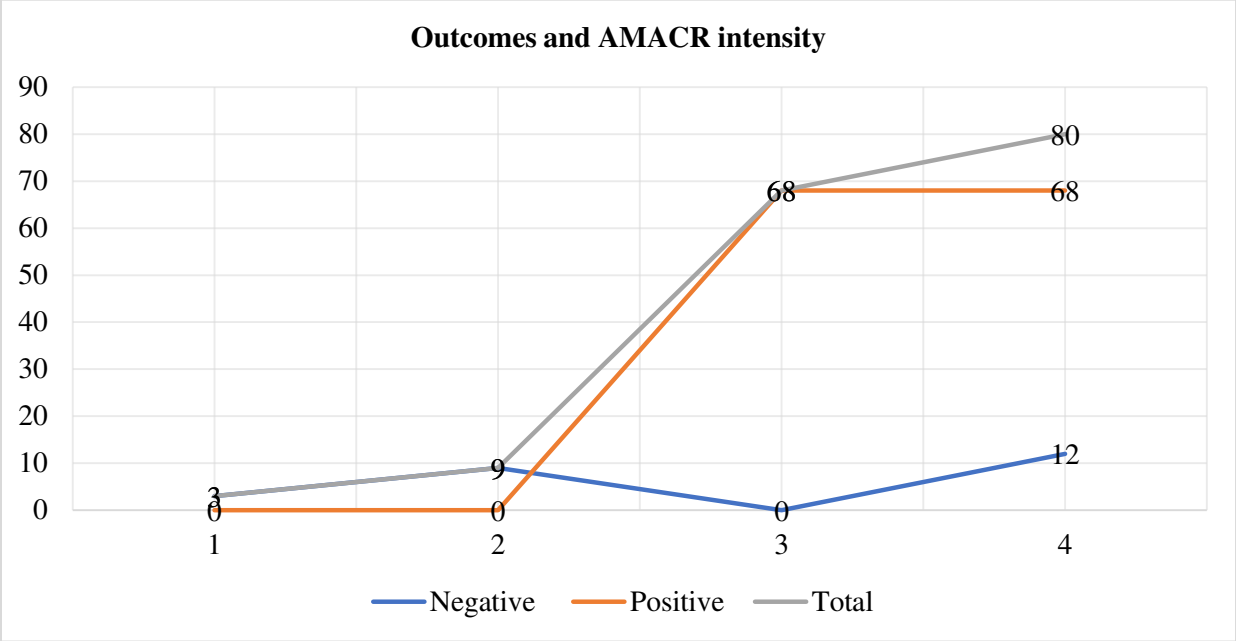


Table – II: Outcomes and AMACR intensity with respect to staining score

Result	Intensity of AMACR Staining Score			Total
	0	1	2	
Negative	3	9	0	12
Positive	0	0	68	68
Total	3	9	68	80



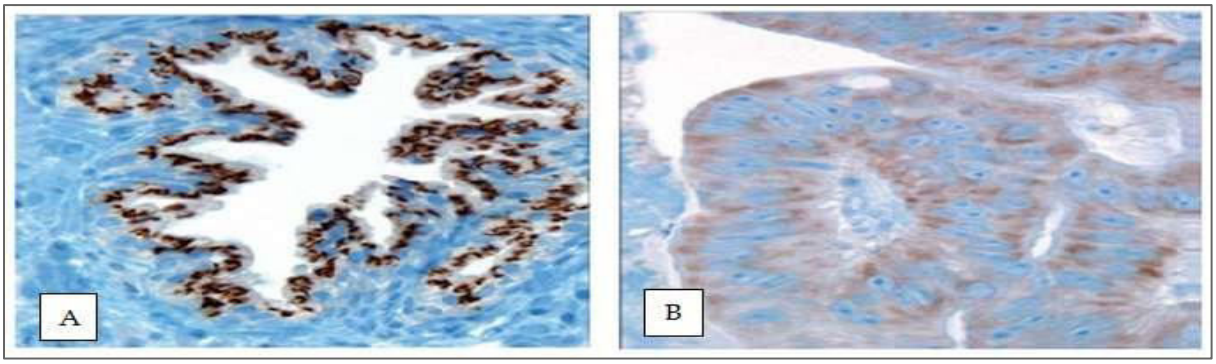


Figure – II: Scoring of cytoplasmic staining AMACR intensity

Prostate cancer incidence in our country is reported as per the factor of age and observed 5.3 in the total of 100,000 males over the year which is also increasing in the recently passed years [3]. The risk of the prostate cancer diagnosis in males is observed as one male in a population of eighty-four in lifespan. Serum prostate is used widely for the specific antigen PSA which is a test of mass screening to diagnose prostate cancer and the outcomes reflect that prostate needle biopsies are increased in number; therefore, there is a need for the improvement of the accurate and pin point diagnostic facility. There is an emergent need for the foe an early carcinoma prostate diagnosis as it is stated in the moderate to advance cancer carcinoma in 40 – 50 percent of the population through final radical prostatectomy [5]. Therefore, the treatment can be delayed because of an underdiagnosis of the limited prostatic adenocarcinoma focus and patients can experience severe consequences. Prostatic cancer diagnosis is a

combination of cytological, architectural and ancillary manifestations. The challenging part is an accurate diagnosis of the tissue as there is presentation of either cancer's small focus or because of the presentation of numerous benign malignancy mimickers such as adenosis. Although basal cell's immunohistochemical stains, including high molecular weight cyto-keratin or currently p63 can be helpful in the focal prostate cancer diagnosis with few restrictions in the utilization. Basal cell marker's negative staining is an automatic carcinoma diagnostic tool. A positive marker of immunohistochemical which is also specific for the prostate cancer is of great importance, it enhances the level of confidence which is mandatory for the definitive diagnosis of the malignancy [6]. Alpha methyl acyl-COA racemase (AMACR) is also referred as (p504s), which is a cytoplasmic enzyme expressed by CDNA microarray which is also overexpressed in number of adenocarcinomas of prostate and in higher prostatic intraepithelial neoplasia, but in other words it is very weak to be expressed in the benign glands. No doubt AMACR is a very useful indicator of the prostate adenocarcinoma as stated in Western countries, in the setting of our country its effective is still is under debate. In the recent research works AMACR specificity and sensitivity for prostate adenocarcinoma diagnosis and Japanese patient's benign glands are less as reported in the past work than the Western countries [7]. In a Japanese research it was observed as (70.6%) against the Western population where it was observed as (95%) [8]. AMACR immunohistochemistry outcomes reflect eighty-five percent positive cases against the Japanese (70.6%), which is observed under the international research outcomes observed in various research studies as 82% & 92% [8, 9]. Yamada has doubts about AMACR specificity as reliable adenocarcinoma prostate positive indicator. However, our outcomes can be compared with any international author outcomes. The variation in the outcomes may be attributed to selection of sample size, selected case types and research methodology.

CONCLUSION:

Positive AMACR staining may be used for the cancer diagnostic through prostate needle core biopsies in the focus of under one-millimeter dimension (taken as maximum). AMACR expression outcomes in this population can be compared with the outcomes of Western research studies. Staining of AMACR need an interpretation in the perspective of basic hematoxylin context and criteria of eosin for malignancy including the outcomes of the related supportive markers expressions which includes a basal cell specified indicator such as 34βE12 or p63.

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