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Research Article

### A STUDY OF ULTRASONOGRAPHIC PATTERN AND HISTOLOGIC OUTCOME OF TRANSRECTAL ULTRASOUND GUIDED BIOPSIES IN PATIENTS WITH PROSTATIC CARCINOMA

<sup>1</sup>Dr. Muhammad Khalid, <sup>2</sup>Dr. Muhammad Ibrahim, <sup>3</sup>Dr. Muhammad Asif,  
<sup>4</sup>Dr. Qadeer Ahmad Tariq

<sup>1</sup>Associate Professor Urology, D.G. Khan Medical College, D.G. Khan.

<sup>2</sup>Medical Officer, DHQ Teaching Hospital, D.G. Khan.

<sup>3</sup>Senior Registrar, DHQ Teaching Hospital, D.G. Khan.

<sup>4</sup>Associate Professor, Urology, Sahiwal Medical College, Sahiwal.

#### Abstract:

**Introduction:** Transrectal ultrasound (TRUS) is one of the modalities for the evaluation of a patient with suspected carcinoma of the prostate. No local study had been done so by conducting this study we assessed the pattern of ultrasonographic findings and their histologic pattern in our local patient population. **Objective:** To find out the ultrasonographic pattern and histologic outcome of transrectal ultrasound guided biopsies in patients with prostatic carcinoma. **Methodology:** This cross sectional study was done at outpatient and Inpatient department of Urology DHQ Teaching Hospital D.G. Khan. Using non-probability consecutive sampling 384 consecutive patients presenting with clinical features or having positive digital rectal examination and fulfilling the inclusion and exclusion criteria were included in the study. All the patients underwent detailed history and physical examination by the researcher. Serum PSA levels was checked in all the patients. The area of abnormality was identified in the peripheral, central or transitional zone as well as the echogenicity of the lesion was noted as hypo/ hyper or isoechoic. 12 core biopsies were taken from the area of abnormality as well as from other standard areas using extended 12 core biopsy technique. These were collected in separate jars, labeled and sent for histopathological analysis. **Results:** The mean age of patients was  $63.20 \pm 7.96$  years. According anatomical zone, 306 (79.7%) patients had peripheral, 18 (4.7%) had central and 60(15.6%) patients had transitional lesion. According to Echogenicity of lesions, 251(65.4%) of the patients had hypoechoic, 126(32.8%) had Isoechoic and 7 (1.8%) patients had hyperechoic echogenicity. According to histological outcome malignancy was present in 308(80.2%) of the patients. **Conclusion:** According to anatomical zone peripheral was the highest lesion followed by transitional and central. Hypoechoic was most followed by Isoechoic and hyperechoic echogenicity in our patients. According to histological outcome malignancy was present in 308(80.2%) of the patients, in which 236 (76.6%) had Peripheral, 16(5.2% had Central and 56(18.2%) patients transitional anatomical zones. Histological outcome (malignancy) was statistically associated with Peripheral anatomical zone, p-value = 0.01.

**Keywords:** Advanced Prostate cancer, transrectal, ultrasound, Anatomical zone, echogenicity Lesion

#### Corresponding author:

**Dr. Muhammad Khalid,**

Associate Professor Urology, D.G. Khan Medical College,  
D.G. Khan.

QR code



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#### INTRODUCTION:

Prostate cancer is the second most common cancer in men worldwide, with an estimated 900,000 cases and 258,000 deaths in 2008 [1]. The prostate gland is divided into three general zones which have shown marked differences in the propensity to harbor prostatic cancer. The clinical behavior of prostate cancer ranges from a microscopic, well-differentiated tumor to an aggressive cancer with high likelihood of invasion and metastasis [2]. Since the introduction of widespread screening using serum PSA, prostate cancer is often diagnosed while asymptomatic. However, screening with serum PSA is controversial, since many of the prostate cancers discovered in this manner may never be clinically significant. In patients not detected by PSA screening, the first evidence of prostate cancer typically is detected either by digital rectal examination (DRE) or due to genitourinary symptoms [3].

On DRE, asymmetric areas of induration or frank nodules are suggestive of prostate cancer. Although prostate cancer can cause urinary urgency, nocturia, frequency, and hesitancy, such symptoms are usually limited to patients with relatively advanced prostate cancer [4].

A histologic examination of tumor is required to establish the diagnosis of prostate cancer. Typically, this is accomplished with a prostate biopsy.<sup>5</sup> While prostate biopsy can be performed with digital guidance, the accuracy of prostate biopsy is greatly improved with transrectal ultrasound (TRUS) guidance, which is easy to perform and generally well-tolerated.<sup>6</sup> Two-dimensional TRUS is typically used for measuring volume and assessing echogenicity of the prostate. The normal prostate has a uniform echotexture. Hypoechoic lesions and those that correlate with an abnormality on digital rectal ultrasound have a higher likelihood of harboring cancer; however, up to one-third of prostate cancers are isoechoic. Hyperechoic areas generally represent areas of prostatic calcification [7].

Multiple sampling schemes have been developed in an effort to improve the accuracy of prostate biopsy in the detection of cancer. Six core or sextant biopsy techniques, was commonly employed taking one sample each from the apex, base, and mid-prostate on each side. However, this method misses about 30 percent of clinically significant cancers and has largely been replaced by extended core biopsy which is performed by obtaining five to seven evenly-distributed specimens from each side, sampling more extensively from the lateral aspects of the prostate.<sup>8</sup>

A systematic review of 87 studies found that an increasing number of cores were significantly associated with increased detection of prostate cancer. Schemes with 12 core samples that took additional laterally directed cores detected 31 percent more cancers (95% CI 25-37) compared to a six-core approach [9].

On TRUS, prostate cancer is visualized as a hypoechoic lesion in 60-70%, and as isoechoic lesion in 30-40% of cases. Hyperechoic lesions are rare, with an incidence of approximately 1.5%. Peripheral zone constitutes approximately 70 percent of the prostate gland and the majority of prostate cancers originate within this zone. Central zone comprises 25 percent of the volume of the normal prostate and contains 5 percent of prostate cancers while transition zone comprises 5 percent of the normal volume of the prostate and is the site of benign prostatic hyperplasia but approximately 10 percent of cancers originate within the transition zone [10].

However, most of this data comes from the western population and there may be racial and geographical differences in the distribution and pattern of malignant lesions within the prostate. By conducting this study we want to assess the pattern of ultrasonographic findings and their histologic pattern in our local patient population.

## MATERIALS AND METHODS

**Study design:** Cross sectional study.

**Setting:** Outpatient and Inpatient department of Urology Nishtar Hospital Multan

**Duration:** Minimum of Six months

**Sample size:** Sample size was 384 patients as calculated by the following formula:

$$n = p(1-p) / d^2, p = 2.3\%, d(\text{margin of error}) = 1.5\%.$$

**Sampling technique:** Non-probability consecutive sampling

## SAMPLE SELECTION

### Inclusion Criteria

1. Male patients.
2. Age 50 to 80 years
3. Positive findings on digital rectal examination.
4. PSA > 4 ng/dL
5. Patients who give their consent to be a part of study.

### Exclusion Criteria

1. Previously diagnosed case of prostatic carcinoma
2. Previous history of prostatic surgery

3. Anal fissure
4. Unwillingness of the patients.

**Data Collection:** Approval from ethical committee of the hospital was sought for maintaining privacy and confidentiality. 384 consecutive patients presenting with clinical features or having positive digital rectal examination and fulfilling the inclusion and exclusion criteria was included in the study. Informed written consent was taken from all the patients. All the patients underwent detailed history and physical examination by the researcher. Serum PSA levels was checked in all the patients. All the patients underwent Transrectal ultrasound was carried out by the consultant urologist with at least 5 years post-graduation experience. The area of abnormality was identified in the peripheral, central or transitional zone as well as the echogenicity of the lesion was noted as hypo/ hyper or isoechoic. 12 core biopsies were taken from the area of abnormality as well as from other standard areas using extended 12 core biopsy technique. These was collected in separate jars, labeled and sent for histopathological analysis. All the data was entered in a specifically designed proforma. All the data was entered in Statistical package for social sciences (SPSS) version 20. Quantitative variable like age of the prostate was calculated as mean and standard deviation. Qualitative data like gender, anatomical zone and echogenicity of the lesion and histological outcome was calculated as frequencies and percentages. Frequencies and percentages were calculated for the presence or absence of malignancy and echogenicities of the lesion. Confounding variables like age and anatomical zone was controlled by stratification. Chi-square test was applied to see the effect of this on outcome. P-value  $\leq 0.05$  was taken as significant.

### RESULTS:

The mean age of patients was  $63.20 \pm 7.96$  years with age range of 37 years. The minimum and maximum age was 50 and 87 years respectively. There were 148 (38.54%) patients whose age was 50-59 years, 168 (43.75%) of patients were 60-69 years old, 55(14.32%) were 70-79 and 13(3.39%) of the patients were 80-89 years of age. The mean  $\pm$  S.E.M PSA level in these patients was  $85.05 \pm 5.16$  with median, minimum and maximum PSA level were 58.75, 4.50 and 573.40 respectively. Note: Here S.E.M (Standard error of mean) is used instead of Standard deviation(S.D) because the was huge variation of data and S.D was greater than Mean PSA. According anatomical zone, 306 (79.7%) patients had peripheral, 18 (4.7%) had central and 60(15.6%) patients had transitional lesion. According to Echogenicity of lesions, 251(65.4%) of the patients had hypoechoic, 126(32.8%) had Isoechoic and 7 (1.8%) patients had hyperechoic echogenicity. According to histological outcome malignancy was present in 308(80.2%) of the patients. Among patients having malignancy, 125 (40.6%) were 50-59 years of age, 136 (44.2%) were 60-69 years of age, 38 (12.3%) were 70-79 years of age and 9(2.9%) were 80-89 years of age. In patient with malignancy, 236 (76.6%) had Peripheral, 16(5.2%) had Central and 56(18.2%) patients Transitional anatomical zones. Histological outcome (malignancy) was statistically associated with Peripheral anatomical zone, p-value = 0.01. Moreover among patients having malignancy, Hypoechoic, Isoechoic and Hyperechoic echogenicity was seen in 195(63.3%), 106 (34.4%) and 7(2.3%) respectively. Statistically there was no association in Echogenicity of the lesion and histological outcome, p-value = 0.139. Anatomical zone and Echogenicity of the lesion were statistically associated, p-value = 0.003.

**Table-1: Frequency distribution of different parameters**

		Frequency	Percent
<b>Anatomical Zone</b>	<b>Peripheral</b>	306	79.7
	<b>Central</b>	18	4.7
	<b>Transitional</b>	60	15.6
<b>Echogenicity of the lesion</b>	<b>Hypoechoic</b>	251	65.4
	<b>Isoechoic</b>	126	32.8
	<b>Hyperechoic</b>	7	1.8
<b>Malignancy on histology</b>	<b>Yes</b>	308	80.2
	<b>No</b>	76	19.8

### DISCUSSION:

Age - adjusted incidence rate in Pakistan is 5.3 per 100,000 person-years, which is slightly lower than India (6.8 per 100,000 person-years), but higher than rates in China (3.1 per 100,000 person-years).<sup>11, 12</sup> Pattern of prostate cancer incidence and mortality suggests that both environmental and lifestyle factors, especially trend of urbanisation and change in socioeconomic status may have accrued the prostate cancer risk in developing countries [12,13].

In Pakistan, population drift towards cities and rising poorly regulated industrialization for the last two to three decades is likely to add new risk factors or modifying the existing deleterious exposures in the community, which in turn may have contributed in growing number of reported prostate cancer cases in Pakistan. Despite high morbidity and mortality, etiology of prostate cancer remains largely unknown. Advancing age, race and family history are the only established risk factors [12,14]. Other risk factors like raised androgen levels, high saturated fat in diet, use of red meat, reduced physical activity and obesity have also been reported but their role in disease causation remains to be explained. Epidemiological studies are consistently documenting that farmers have around 10% excess risk of developing prostate cancer. This may be due to exposure to insecticides and pesticides [12,15].

Prostate specific antigen (PSA) is a protease which is characteristic of the prostate. It is widely used as a serum marker for the early diagnosis of prostate cancer (PCa). Nevertheless, for concentrations between 4 and 10 ng/mL, PSA does not enable PCa to be distinguished from benign diseases, such as benign prostate hyperplasia (BPH). In sera, the use of a ratio between free PSA (PSA uncomplexed with protease inhibitor) and total PSA (free PSA and PSA bound to alpha-1 anti-chymotrypsin) enables the gray zone to be reduced, but an important proportion of patients are still wrongly classed. Using two-dimensional electrophoresis, we demonstrated using 52 PCa and 40 BPH well-documented clinical cases that BPH sera show a significantly greater percentage of low-molecular-weight free PSA elements (IwPSA) than PCa sera.<sup>16</sup>

Here in this study the mean  $\pm$  S.E.M PSA level in these patients was  $85.05 \pm 5.16$  with median, minimum and maximum PSA level were 58.75, 4.50 and 573.40 respectively.

Prostate cancer is now increasingly diagnosed at an early stage following the introduction of the biomarker Prostate specific antigen and the

possibility of accurate biopsy guided by state of the art TRUS facility.<sup>17-19</sup> In the developing countries, late clinical disease is still the commonest mode of presentation [20].

We found that The mean age of patients was  $63.20 \pm 7.96$  years with age range of 37 years. The minimum and maximum age was 50 and 87 years respectively. There were 148 (38.54%) patients whose age was 50-59 years, 168 (43.75%) of patients were 60-69 years old, 55(14.32%) were 70-79 and 13(3.39%) of the patients were 80-89 years of age.

In a recent study, majority of the patients (45%) were mainly in their seventh decade (60-69 years) of life with a mean age was 66.3 years [10]. This is similar to the mean age reported by DN Osegbe (68 years) and by Dawam and colleagues (66.3 years) in their studies on Nigerians [21,22]. Our findings are almost similar to above findings.

The recruitment of patients thought to have advanced disease in this study probably accounts for the high specificity found. All the prostates with hyperechoic and most of those with isoechoic appearance had benign histology, but this is not surprising because findings from other studies show that they account for only 1-14% of prostate cancer.<sup>23</sup> Ellis and co-workers noted that 37.6% of the cancers were diagnosed in isoechoic areas of the prostate<sup>24</sup>, while Flanigan and associates found that only 18% of 855 sonographically suspicious quadrants actually contained cancer on biopsy, whereas 65% of normal looking quadrants contained cancer and 17% of hypoechoic areas yielded cancer [25]. A study reported the mean prostate size was 66.8 g with a range 15-219 g; this may not contribute much in differentiating benign from malignant prostate.<sup>10</sup> The ultrasound features were mostly of mixed echogenicity (39.7%), followed by hypoechoic nodules (22.1%) [26]. In current study according anatomical zone, 306 (79.7%) patients had peripheral, 18 (4.7%) had central and 60(15.6%) patients had transitional lesion. According to Echogenicity of lesions, 251(65.4%) of the patients had hypoechoic, 126(32.8%) had Isoechoic and 7 (1.8%) patients had hyperechoic echogenicity.

Cancer can be detected more often in patients with TRUS findings of hypoechoic nodules (56.3%).<sup>10</sup> It is also suggested a higher positive predictive value for cancer using TRUS findings, studies have shown that they generally lack specificity with a low positive predictive value of <28% [18]. In current study we

found on TRUS guided histological outcome malignancy was present in 308(80.2%) of the patients, that is higher as compare to above cited study. This has made TRUS findings an unreliable tool in prostate cancer screening, while on the other hand, it has markedly improved prostate biopsy guidance [10].

### CONCLUSION:

According to anatomical zone peripheral was the highest lesion followed by transitional and central. Hypoechoic was most followed by Isoechoic and hyperechoic echogenicity in our patients. According to histological outcome malignancy was present in 308(80.2%) of the patients, in which 236 (76.6%) had Peripheral, 16(5.2% had Central and 56(18.2%) patients transitional anatomical zones. Histological outcome (malignancy) was statistically associated with Peripheral anatomical zone, p-value = 0.01. Moreover among patients having malignancy, Hypoechoic, Isoechoic and Hyperechoic echogenicity was seen in 195(63.3%), 106 (34.4%) and 7(2.3%) respectively. Anatomical zone and Echogenicity of the lesion were statistically associated, p-value = 0.003. Hence TRUS guided biopsy can be used to diagnose prostate carcinoma and more studies are needed to confirm our results.

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