# EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE

BY
DR. AYSWARIA PADMAJA UNNITHAN, MBBS

**DISSERTATION SUBMITTED TO**
**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION &RESEARCH**
**TAMAKA, KOLAR, KARNATAKA**
**IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF**

**DOCTOR IN MEDICINE**
**IN**
**PATHOLOGY**

**UNDER THE GUIDANCE OF**
**DR. SUBHASISH DAS,** MD
**PROFESSOR**

**DEPARTMENT OF PATHOLOGY DEPARTMENT OF PATHOLOGY**

**SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR**

**JUNE 2023**

# SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH,

# TAMAKA, KOLAR, KARNATAKA

## DECLARATION BY THE CANDIDATE

I HEREBY DECLARE THAT THIS DISSERTATION ENTITLED

**"EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE.**

**DONE IN SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR**

IS A BONAFIDE AND GENUINE RESEARCH WORK CARRIED OUT BY ME UNDER THE DIRECT GUIDANCE OF

**Dr. SUBASHISH. DAS**

**PROFESSOR,**

**DEPARTMENT OF PATHOLOGY,**

**SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR**

DATE:

PLACE: KOLAR

SIGNATURE OF THE CANDIDATE

**Dr. AYSWARIA PADMAJA UNNITHAN**

# SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH,

# TAMAKA, KOLAR, KARNATAKA.

## CERTIFICATE BY THE GUIDE

THIS IS TO CERTIFY THAT THE DISSERTATION ENTITLED

**"EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE."**

**DONE IN SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR**

IS A BONAFIDE RESEARCH WORK DONE

BY

**Dr. AYSWARIA PADMAJA UNNITHAN**

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

**M.D IN PATHOLOGY**

DATE:

PLACE: KOLAR

SIGNATURE OF THE GUIDE

**Dr. SUBASHISH. DAS**
**PROFESSOR**
**DEPARTMENT OF PATHOLOGY**

# SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH,

# TAMAKA, KOLAR, KARNATAKA

## CERTIFICATE BY THE CO-GUIDE

THIS IS TO CERTIFY THAT THE DISSERTATION ENTITLED

**"EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE ."**

**DONE IN SRI DEVARAJ URS MEDICAL COLLEGE,**

**KOLAR**

IS A BONAFIDE RESEARCH WORK DONE

BY

**Dr. AYSWARIA PADMAJA UNNITHAN**

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

**M.D IN PATHOLOGY**

DATE:

PLACE: KOLAR

SIGNATURE OF THE CO-GUIDE

**DR. P.N.SREERAMULU**
DEPARTMENT OF SURGERY
SRI DEVARAJ URS MEDICAL COLLEGE,TAMAKA ,KOLAR

# SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH,

# TAMAKA, KOLAR, KARNATAKA.

## ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

THIS IS TO CERTIFY THAT THE DISSERTATION ENTITLED

**"EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE."**

IS A BONAFIDE RESEARCH WORK DONE BY

**Dr. AYSWARIA PADMAJA UNNITHAN**

UNDER THE GUIDANCE OF

**DR. SUBASHISH. DAS, MBBS MD**

PROFESSOR

DEPARTMENT OF PATHOLOGY

**Dr. KALYANI. R**

SEAL & SIGNATURE OF THE HOD

DATE:

PLACE: KOLAR

**Dr. P.N.SREERAMULU**

SEAL & SIGNATURE OF THE PRINCIPAL

DATE:

PLACE: KOLAR

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH,**

**TAMAKA, KOLAR, KARNATAKA.**

.

## COPYRIGHT

## DECLARATION BY THE CANDIDATE

I HEREBY DECLARE THAT

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

SHALL HAVE THE RIGHTS TO PRESERVE, USE AND DISSEMINATE

THIS DISSERTATION,

IN PRINT OR ELECTRONIC FORMAT, FOR ACADEMIC / RESEARCH PURPOSE.

DATE: SIGNATURE OF THE CANDIDATE

PLACE: KOLAR **Dr. AYSWARIA PADAMAJA UNNITHAN**

# SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH,

# TAMAKA, KOLAR, KARNATAKA.

## ETHICS COMMITTEE

# CERTIFICATE

THIS IS TO CERTIFY THAT, THE ETHICS COMMITTEE OF

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR

HAS UNANIMOUSLY APPROVED

**Dr. AYSWARIA PADMAJA UNNITHAN**

POST GRADUATE STUDENT IN THE DEPARTMENT OF PATHOLOGY OF

SRI DEVARAJ URS MEDICAL COLLEGE

TO TAKE UP THE DISSERTATION WORK ENTITLED

**"EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE.**

TO BE SUBMITTED TO
SRI DEVARAJ URS ACADEMY OF

HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR.

**MEMBER SECRETARY** **PRINCIPAL**

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH

**SRI DEVARAJ URS MEDICAL COLLEGE**

Tamaka, Kolar

**INSTITUTIONAL ETHICS COMMITTEE**

**Members**

1. **Dr. D.E.Gangadhar Rao, (Chairman)** Prof. & HOD of Zoology, Govt. Women's College, Kolar
2. **Dr. Sujatha.M.P, (Member Secretary),** Prof. Department of Anesthesia, SDUMC
3. Mr. Gopinath Paper Reporter, Samyukth Karnataka
4. Mr. G. K. Varada Reddy Advocate, Kolar
5. Dr. Hariprasad S, Assoc. Prof Dept, of Orthopedics, SDUMC
6. Dr. Abhinandana R Asst. Prof. Dept. of Forensic Medicine, SDUMC
7. Dr. Ruth Sneha Chandrakumar Asst. Prof. Dept. of Psychiatry, SDUMC
8. Dr. Usha G Shenoy, Asst. Prof., Dept. of Allied Health & Basic Sciences SDUAHER
9. Dr. Munilakshmi U Asst. Prof. Dept. of Biochemistry, SDUMC
10. Dr.D.Srinivasan, Assoc. Prof. Department of Surgery, SDUMC
11. Dr. Waseem Anjum, Asst. Prof. Department of Community Medicine, SDUMC
12. Dr. Shilpa M D Asst. Prof. Department of Pathology, SDUMC

**No. SDUMC/KLR/IEC/ 565(a) /2020-21 Date: 24.12.2020**

## PRIOR PERMISSION TO START OF STUDY

The Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has examined and unanimously approved the study entitled **"Expression of bax and BCL2 in Prostate Carcinoma and its Correlation with Gleason Score"** being investigated by **Dr. Ayswaria Padmaja Unnithan,** Dr. Subhashis Das & Dr. Sreeramulu P N[1] in the Departments of Pathology & Surgery[1] at Sri Devaraj Urs Medical College, Tamaka, Kolar. **Permission is granted by the Ethics Committee to start the study**.

Sujatha. M.P

Member Secretary

Member Secretary
Institutional Ethics Committee
Sri Devaraj Urs Medical College
Tamaka Kolar.

Chairman

CHAIRMAN
Institutional Ethics Committee
Sri Devaraj Urs Medical College
Tamaka, Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH

Tamaka, Kolar 563103

## Certificate of Plagiarism Check

| | |
|---|---|
| **Title of the Thesis/Dissertation** | EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE |
| **Name of the Student** | DR.AYSWARIA UNNITHAN |
| **Registration Number** | 20PA1096 |
| **Name of the Supervisor / Guide** | Dr. SUBHASHISH DAS |
| **Department** | PATHOLOGY |
| **Acceptable Maximum Limit (%) of Similarity** (PG Dissertation /Ph.D. Thesis) | 10% |
| **Similarity** | 4% |
| **Software used** | Turnitin |
| **Paper ID** | 1991044255 |
| **Submission Date** | 11/01/2023 |

**Signature of Student**

**Signature of Guide/Supervisor**

Professor
Department of Pathology
Sri Devaraj Urs Medical College
Tamaka, Kolar-563101.

**HOD Signature**

Professor and Head
Department of Pathology
Sri Devaraj Urs Medical College
Tamaka, Kolar-563101

**University Librarian**

University Library
Learning Resource Centre
SDUAHER, Tamaka
KOLAR-563103

**Coordinator UG and PG Program**

Co-Ordinator,
UG&PG Program ,Faculty of Medicine,
Sri Devarj Urs Medical College ,
Tamaka, Kolar- 563103

turnitin

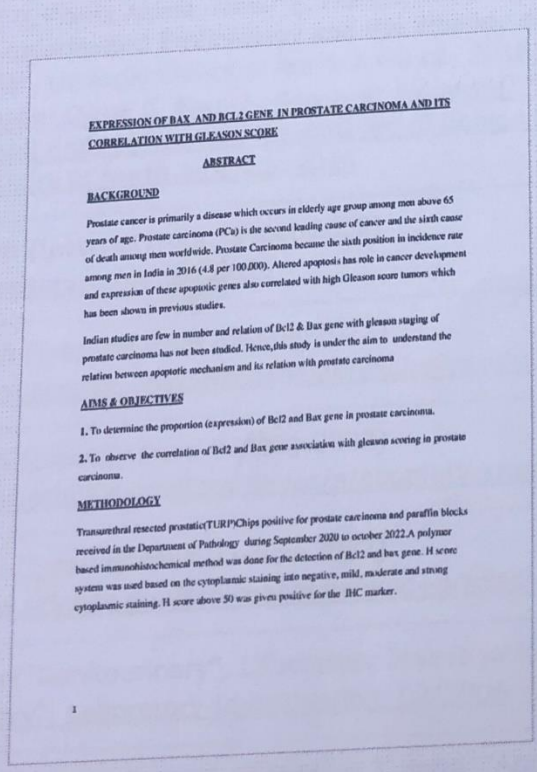
# Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

| | |
|---|---|
| Submission author: | Ayswaria Unnithan |
| Assignment title: | PG dissertation 2023 |
| Submission title: | EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINO... |
| File name: | final_thesis_FOR_PLAG_CORRECTION_1.docx |
| File size: | 9.97M |
| Page count: | 75 |
| Word count: | 4,774 |
| Character count: | 24,383 |
| Submission date: | 11-Jan-2023 08:51AM (UTC+0530) |
| Submission ID: | 1991044255 |

Professor
Department of Pathology
Sri Devaraj Urs Medical Col
Tamaka, Kolar-56310



**EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE**

**ABSTRACT**

**BACKGROUND**

Prostate cancer is primarily a disease which occurs in elderly age group among men above 65 years of age. Prostate carcinoma (PCa) is the second leading cause of cancer and the sixth cause of death among men worldwide. Prostate Carcinoma became the sixth position in incidence rate among men in India in 2016 (4.8 per 100,000). Altered apoptosis has role in cancer development and expression of these apoptotic genes also correlated with high Gleason score tumors which has been shown in previous studies.

Indian studies are few in number and relation of Bcl2 & Bax gene with gleason staging of prostate carcinoma has not been studied. Hence,this study is under the aim to understand the relation between apoptotic mechanism and its relation with prostate carcinoma

**AIMS & OBJECTIVES**

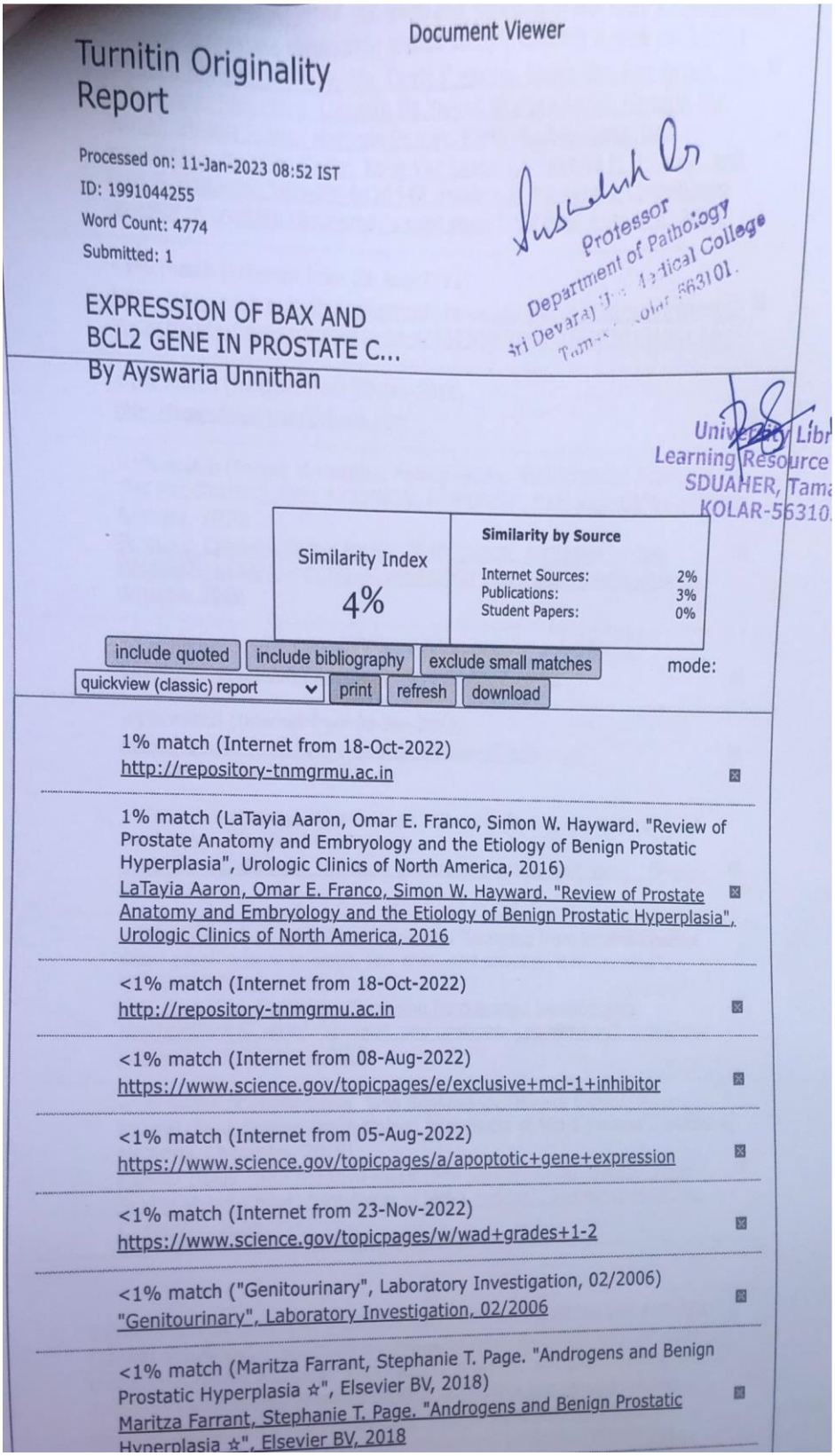
1. To determine the proportion (expression) of Bcl2 and Bax gene in prostate carcinoma.

2. To observe the correlation of Bcl2 and Bax gene association with gleason scoring in prostate carcinoma.

**METHODOLOGY**

Transurethral resected prostatic(TURP)Chips positive for prostate carcinoma and paraffin blocks received in the Department of Pathology during September 2020 to october 2022.A polymer based immunohistochemical method was done for the detection of Bcl2 and bax gene. H score system was used based on the cytoplasmic staining into negative, mild, moderate and strong cytoplasmic staining. H score above 50 was given positive for the IHC marker.

1



Document Viewer

# Turnitin Originality Report

Processed on: 11-Jan-2023 08:52 IST
ID: 1991044255
Word Count: 4774
Submitted: 1

EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE C...
By Ayswaria Unnithan

Professor
Department of Pathology
Sri Devaraj [illegible] Medical College
Tam[illegible] Kolar 563101.

University Library
Learning Resource
SDUAHER, Tamaka
KOLAR-563101

| Similarity Index | Similarity by Source | |
|---|---|---|
| 4% | Internet Sources: | 2% |
| | Publications: | 3% |
| | Student Papers: | 0% |

include quoted | include bibliography | exclude small matches | mode:
quickview (classic) report | print | refresh | download

1% match (Internet from 18-Oct-2022)
http://repository-tnmgrmu.ac.in

1% match (LaTayia Aaron, Omar E. Franco, Simon W. Hayward. "Review of Prostate Anatomy and Embryology and the Etiology of Benign Prostatic Hyperplasia", Urologic Clinics of North America, 2016)
LaTayia Aaron, Omar E. Franco, Simon W. Hayward. "Review of Prostate Anatomy and Embryology and the Etiology of Benign Prostatic Hyperplasia", Urologic Clinics of North America, 2016

<1% match (Internet from 18-Oct-2022)
http://repository-tnmgrmu.ac.in

<1% match (Internet from 08-Aug-2022)
https://www.science.gov/topicpages/e/exclusive+mcl-1+inhibitor

<1% match (Internet from 05-Aug-2022)
https://www.science.gov/topicpages/a/apoptotic+gene+expression

<1% match (Internet from 23-Nov-2022)
https://www.science.gov/topicpages/w/wad+grades+1-2

<1% match ("Genitourinary", Laboratory Investigation, 02/2006)
"Genitourinary", Laboratory Investigation, 02/2006

<1% match (Maritza Farrant, Stephanie T. Page. "Androgens and Benign Prostatic Hyperplasia ☆", Elsevier BV, 2018)
Maritza Farrant, Stephanie T. Page. "Androgens and Benign Prostatic Hyperplasia ☆", Elsevier BV, 2018

# ACKNOWLEDGEMENT

I begin by expressing my immense gratitude to the Almighty Lord for his blessings. My continued reverence and acknowledgment to the beloved teacher and guide **Dr. Subhashish Das**, Professor of Pathology, who handpicked this topic and graced study officially with her constant support and expert advice, her encouragement, wise constructive judgment the painstaking effort to weed out errors, and her affection during study leave permanently indebted to her. I dedicate a good part of the work to her.

Sincere thanks to **Dr. P. N. Sreeramulu**, Professor of Surgery and Dean, Faculty of Medicine, to consent to be the co-guide and give timely help throughout the PG career.

I take this opportunity to express my humble and sincere gratitude and indebtedness to the teacher **Dr. Kalyani R**, Professor and Head of the Department, for her expert advice, constant support, encouragement, and timely help in every aspect.

I would like to express my gratitude to **Dr. Harendra Kumar M.L,** Professor, & **Dr.CSBR Prasad** , Professor for his constant guidance, support, and encouragement..

I express my deep, immense gratitude and humble thanks to **Dr. T.N. Suresh,** Professor. For his support, advice, and encouragement.

I express my deep, immense gratitude and humble thanks to **Dr.Hemalatha.A**, Professor, for his advice and encouragement throughout the study.I want to convey my sincere thanks to **Dr. Manjula K**, Professor, **Dr. Swaroop Raj B.V,** and **Dr. Sushan Shweta Jayekar**, Associate Professors, for their kind help, constant support, and expert advice in preparing this dissertation.

I express my sincere thanks to associate professors **Dr. Supreetha M S** & **Dr. Shilpa M D**, and **Dr. Sindhu C and Dr. Haritha**, Assistant Professors, for their constant guidance and encouragement in preparing this dissertation.

My family **Dr.Vivek MP (**my husband**)** will always be the most significant source of strength and inspiration for their unconditional support in every aspect of life. I am infinetly thankfull to my father **G S Unnithan**, mother **Dr Padmaja Unnithan** and my brother **Abhishek Unnithan** whom I am forever indebted.

I express my sincere thanks to my batchmates and friends, **Dr.Ankita, Dr.Sudarshan, Dr.Snigdha, Dr.Amrutha, Dr.Jahnavi, Dr Satadruti, Dr Nagaraj** for their support and love in every aspect of life. I express my immense gratitude and special thanks to seniors **Dr. Priyanka, Dr.Gaurav, Dr.Sonia, Dr.Ankit, Dr. Nikhil, Dr. Princy, Dr.Soumya and Dr. Soujanya** for their support.

I enjoyed working with my juniors –**Dr. Deepika, Dr.Divya, Dr.Queen Mary, Dr.Haneena, Dr.Ambika, Dr.Sahiti, Dr.Priyanka, Dr.Zubiya, Dr.Manju, Dr.Kamala, Dr.Nikitha, Dr.Sushma, Dr.Prathibha, Dr.Sarju, Dr.Bhadra, Dr.Deepa.** I thank you for your kind cooperation.

. I am thankful to technical staff Mr Veerendra, Mr Shankar, Mrs.Asha ,Mrs.Sumathi.Mr Muthuswamy, Mrs kavitha ,Mr Bhaskar ,Mr Ravi, Mrs Gandharbha, Mrs Surekha, Mrs Roopa ,Mrs Sarada and all non-teaching staff for their invaluable help, without whom this study would not have been possible.

Thank you, everyone.

Date : Signature of the Candidate

Place: KOLAR **Dr. Ayswaria Padmaja Unnithan**

## LIST OF ABBREVATIONS

Pca- Prostate Carcinoma

ISUP-International System for Urologic Pathology

PBCRs-population-based cancer registries.

IL- Interleukins

TGF- Tumor Growth Factor

TNF- Tumor Necrosis Factor

VEGF- Vascular Endothelial Growth Factor

BPH- Benign Prostatic Hyperplasia.

UGS- Urogenital Sinus.

PSA- Prostate specific antigen

PSAP- Prostate-Specific Acid Phosphatase (PSAP)

DRE- Digital rectal exam

AUA- American Urologic Association Recommendations

AJCC- American Joint Committee on Cancer Prognostic Stage Grouping of prostatic carcinoma

TURP-Transurethral resected prostatic(TURP)

# EXPRESSION OF BAX AND BCL2 GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORE


## ABSTRACT

### BACKGROUND

Prostate cancer is primarily a disease which occurs in elderly age group among men above 65 years of age. Prostate carcinoma (PCa) is the second leading cause of cancer and the sixth cause of death among men worldwide. Prostate Carcinoma became the sixth position in incidence rate among men in India in 2016 (4.8 per 100,000). Altered apoptosis has role in cancer development and expression of these apoptotic genes also correlated with high Gleason score tumors which has been shown in previous studies.

Indian studies are few in number and relation of Bcl2 & Bax gene with gleason staging of prostate carcinoma has not been studied. Hence,this study is under the aim to understand the relation between apoptotic mechanism and its relation with prostate carcinoma

### AIMS & OBJECTIVES

**1.** To determine the proportion (expression) of Bcl2 and Bax gene in prostate carcinoma.

**2.** To observe the correlation of Bcl2 and Bax gene association with gleason scoring in prostate carcinoma.

### METHODOLOGY

Transurethral resected prostatic(TURP)Chips positive for prostate carcinoma and paraffin blocks received in the Department of Pathology during September 2020 to october 2022.A polymer based immunohistochemical method was done for the detection of Bcl2 and bax gene. H score system was used based on the cytoplasmic staining into negative, mild, moderate and strong cytoplasmic staining. H score above 50 was given positive for the IHC marker.

**RESULTS**

A total of 50 cases were studied and most of the patients fall in age group of 61-70 years. In the present study, majority of the cases was in Gleason grade 5(42%), PSA levels was in range 90-99(28%), tumor size in range of 3.1-6 cm (44%), T4 stage (34%) ,metastasis (80%).There was remarkable relationship between Gleason grade and tumor size & levels of PSA were in increasing manner with Gleason s grade except at 3rd grade and was significant. There was remarkable relationship between Gleason grade and H-score Bcl2 , suggesting the contribution of bcl2 to development of tumor cells , but not significant with bax gene

**CONCLUSION**

This study concluded that PSA levels in cases of prostate cancer patients were showing increasing trend with Gleasons grade and found to be significant on ANOVA test. It also showed there was remarkable relationship between Gleason grade and H score BCL2, but not that significant with Bax gene.

As there is moderate increase PSA levels with increasing Gleason grade, which reveals higher levels predict the severity and prognosis of prostate cancer. BCL2 expression which is more common in tumor tissues & linked to higher advanced Gleason grade, Furthur studies on the association of these anti apoptotic and pro apoptotic proteins with prostate cancer cases can pave the way for the advanced treatment for the patients in future.

**Keywords**-PSA, prostate carcinoma, Gleason score, Bcl2 and Bax gene, altered apoptosis

# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF CHARTS

## LIST OF PICTURES

# INTRODUCTION

# INTRODUCTION

Prostate carcinoma (PCa) is the second leading cause of cancer and the sixth cause of death among men worldwide.[1] Among 1.4 lakh new Prostate Carcinoma cases which were diagnosed globally in 2020, with age-standardized rate (ASR) incidence of 31 per 1 lakh. South-Central Asia had the lowest ASR (6.3), whereas Northern Europe had the highest all-age incidence ASR (83).[2] Prostate cancer is primarily a disease which occurs in elderly age group among men above 65 years of age.[3]

Restricted data available from previous studies on prostate carcinoma showing huge differences in incidence , characterstics of the diseases and preciptating factors of prostate carcinoma.[3] In India, true incidence of prostatic carcinoma is difficult to estimate as it does not come under most reported disease and less number of population-based cancer registries [PBCRs] noted among Indian population.[3]Annual Percentage Change of Karnataka is 3.4% according to study done considering PBCR during the time period 2009-2011 in various metro cities in India .[3]

With a considerable rise in age-standardized incidence rate of 29.8% from 1990 to 2016, Prostate Carcinoma became the sixth position in incidence rate among men in India in 2016 (4.8 per 100,000).[4] Population-based cancer registries demonstrate a steady and quick growth, refuting the idea that Prostate Cancer incidence in India is lower than in the West[4].

The clinical behaviour of prostate cancer varies, ranging from slow-growing tumours to deadly malignancies that are aggressive.[5,6,7] Clinical stage, grade, and pre treatment blood levels of prostate-specific antigen (PSA) are clinical prognostic variables that forecast recurrence following therapy (PSA).[8]

A mechanism for removing damaged cells through a process called apoptosis is present in almost all tissues. Programmed cell death disruption can result in the buildup of cells with damaged genomes and, ultimately, cancer.[9] Tumour suppressor gene p53 and BCL2 group of genes are

two examples of the genes that control apoptosis. Anti-apoptotic (like Bcl-2 and Bcl-xL) and pro-apoptotic (like Bax, BAK, and BIM) proteins belong to Bcl-2 family.[10]

Using tissue samples from a prostate biopsy, the Gleason grading system was used to assess the prognosis of individuals with prostate cancer. Study conducted in kolar on prostate cancer cases revealed 2.58% among all other cancers.[11,12] Based on how the appearance under a microscope, Gleason score can be assigned in case of prostate cancer.[13]

The International Society of Urologic Pathology (ISUP) made a considerable modification of the Gleason grading system for prostate cancer in 2014 from its original 1960s–1970s scheme. As one of the most important considerations for choosing a course of therapy, the Gleason grading system has been integrated into World Health Organisation (WHO) classification of prostate cancer, the AJCC/UICC staging system, and National Comprehensive Cancer Network (NCCN) recommendations.[14]

## NEED FOR THE STUDY

Some investigations have recommended that altered apoptosis has role in cancer development and expression of these apoptotic genes also correlated with high Gleason score tumors.[15-18] Most of the studies done on these associations are not from india, and the existing data is very sparse. Hence present study aimed at association between expression of BAX & BCL2 gene with gleason scoring which was updated in 2016 for prostate carcinoma.

.

# AIMS & OBJECTIVES

# AIMS & OBJECTIVES

1. To determine the proportion (expression) of Bcl2 and Bax gene in prostate carcinoma.
2. To observe the correlation of Bcl2 and Bax gene association with gleason scoring in prostate carcinoma.

# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

## EMBRYOLOGY

The prostate is an organ of walnut size which is seen at the base of the urinary bladder. It is the core of three major causes of morbidity; prostatitis, benign prostatic hyperplasia (BPH) and prostate carcinoma Embryo has the capacity to develop towards a female or male phenotype. At conception this will be determined and the Mullerian ducts , Wolffian ducts, the urogenital sinus (UGS) and the fetal gonad will be formed. Fetal gonads produce hormones like androgens , male sexual differentiation will take place by mullerian duct regression[15].

The prostate form in 50 mm human embryos from the walls of USG at Mullerian tubercle site epithelial buds growing laterally. Solid branching cords are formed by these buds and develop a lumen which will give rise tubules and alveoli network[16]..

The growth and development of the prostate starts with prostatic buds formation from UGS foetus and at sexual maturity, it would get completed.[17]

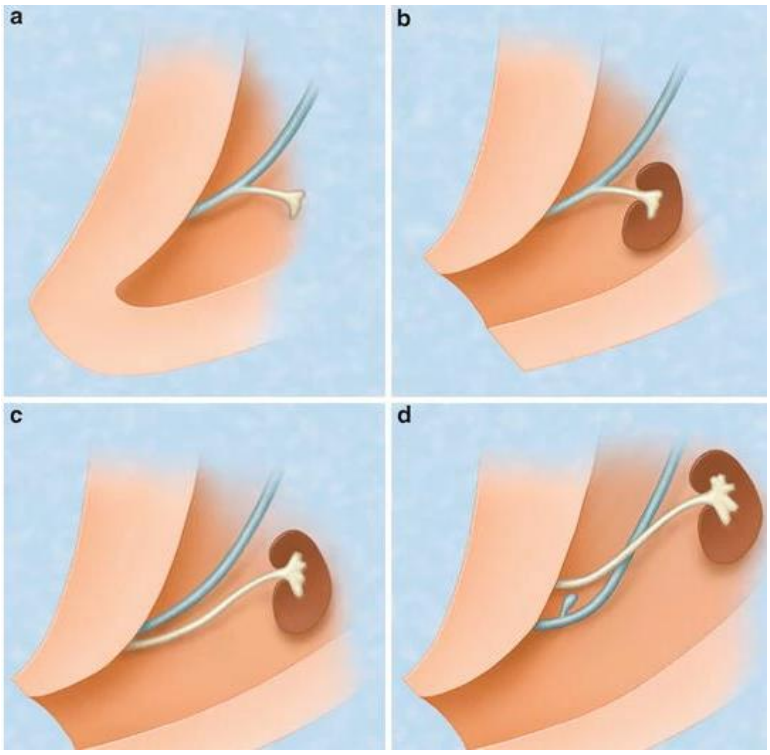



**Fig I-Normal development of Seminal vesicles and Vas Deferens.**

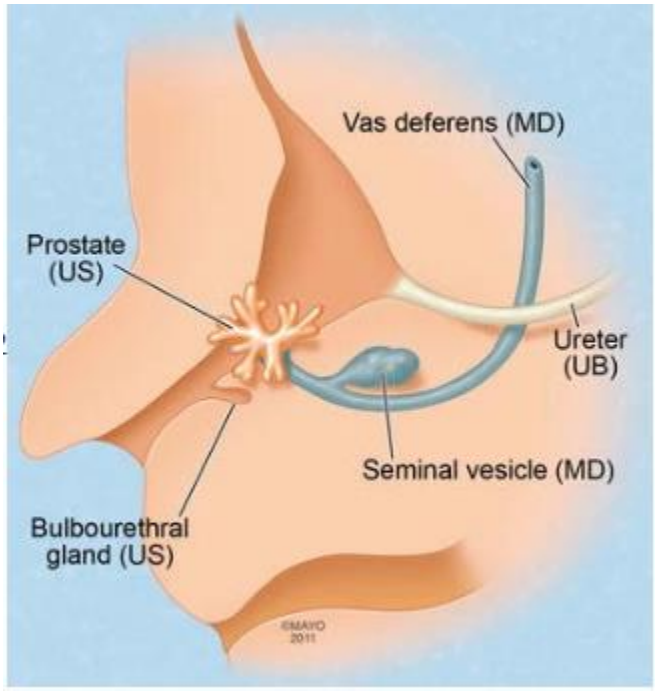



**Fig 2-Development of prostate and Cowper s glands from urogenital sinus.**

## ANATOMY[18]

In normal adult male the prostate weighs up to 20 g and for subsequent growth and its differentiation it depends for and on androgenic hormones synthesized in the testis. It is divided into the fibro muscular stroma and three glandular zones which are distinct mentioned by McNeal: peripheral zone, transition zone, central zone.

**The transition zone**: which surrounds the urethra in the prostate mid portion and the anatomic region which gets enlarged by benign prostatic hyperplasia.

**The central zone:** is shape of an inverted pyramid at prostate base and consist of ejaculatory ducts as they pave the way to the prostatic urethra at the verumontanum, a posterior prominence which is noted in the prostatic urethra. The central zone which has prostatic glands may have a unique morphology with more deeply eosinophilic cytoplasm and more complex intraluminal architecture consisting of papillary infolding or epithelial bridges

**The peripheral zone**: which envelopes the transition zone (TZ) and caudally it extends to comprise most of the apex. Finally, the anterior tissues consist of smooth muscle, skeletal muscle from the anterior fibro muscular sling , and adipose tissue in the extra prostatic compartment

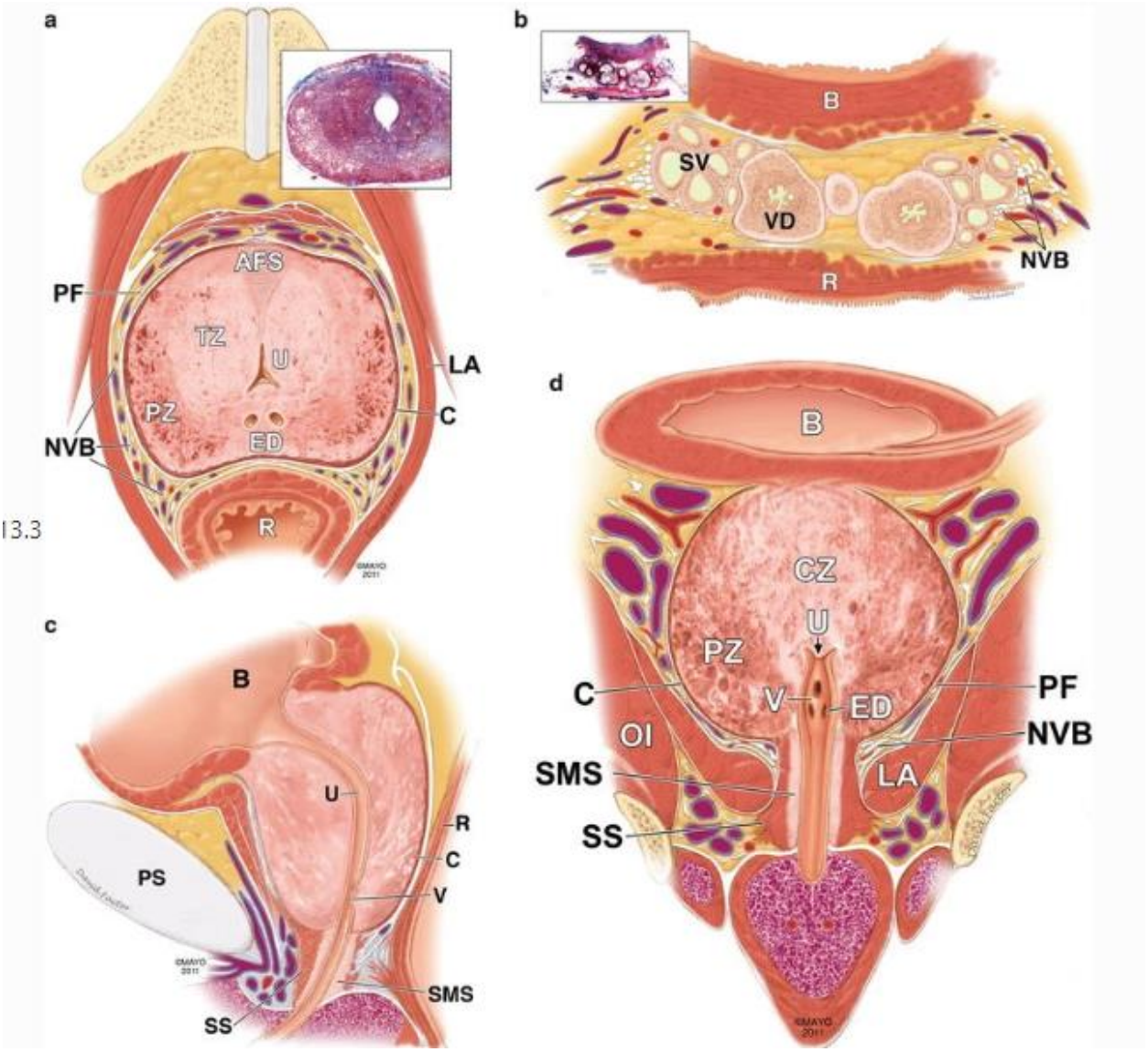



**Fig 3-Normal anatomy of prostate and seminal vesicles.**

## HISTOLOGY:

The glandular component of the prostate is divided into acini and ducts. Secretory cells are noted on the luminal side which, donate a vast variety of products to the seminal fluid. these cells form an undulating luminal surface and are characterized by relatively pale cytoplasm.. The basal cells form a thin layer and separates the luminal secretory cells from the basement membrane.[18]

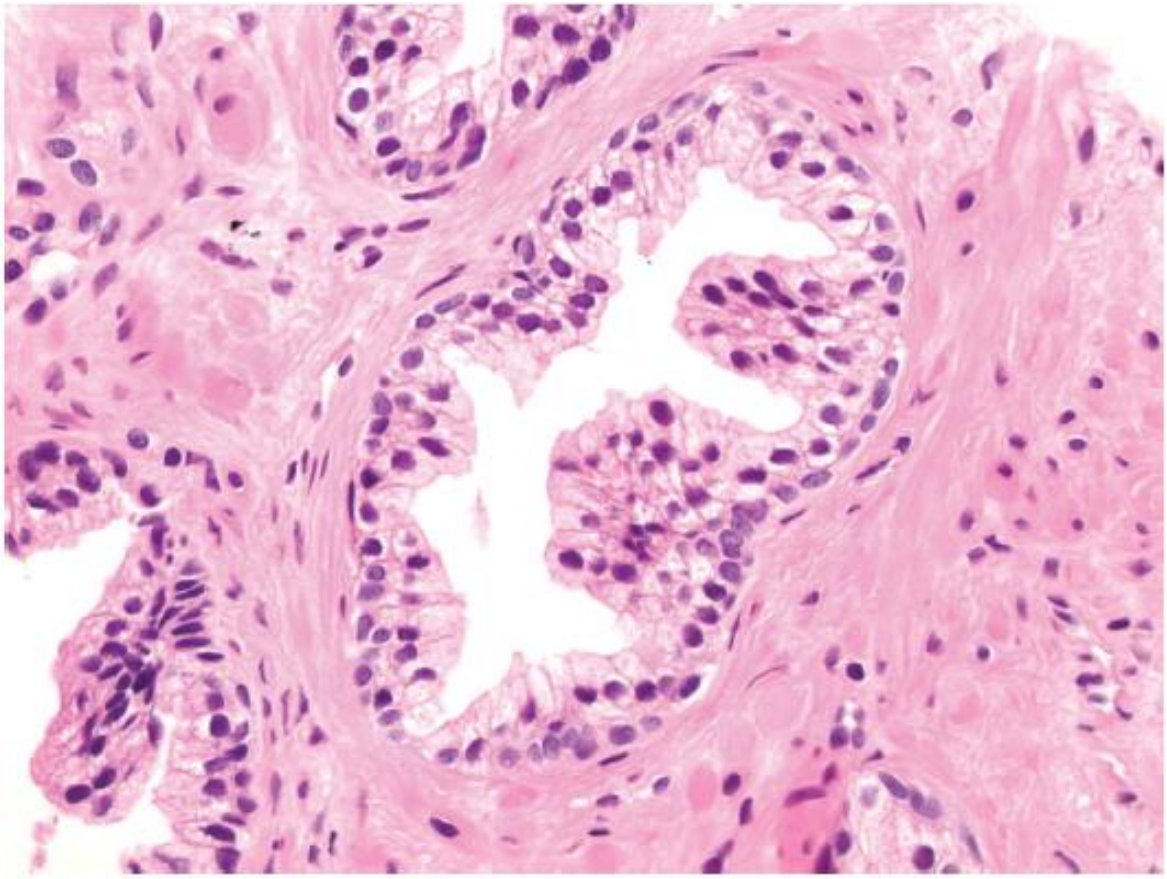


**Fig 4- Normal histology of prostate**

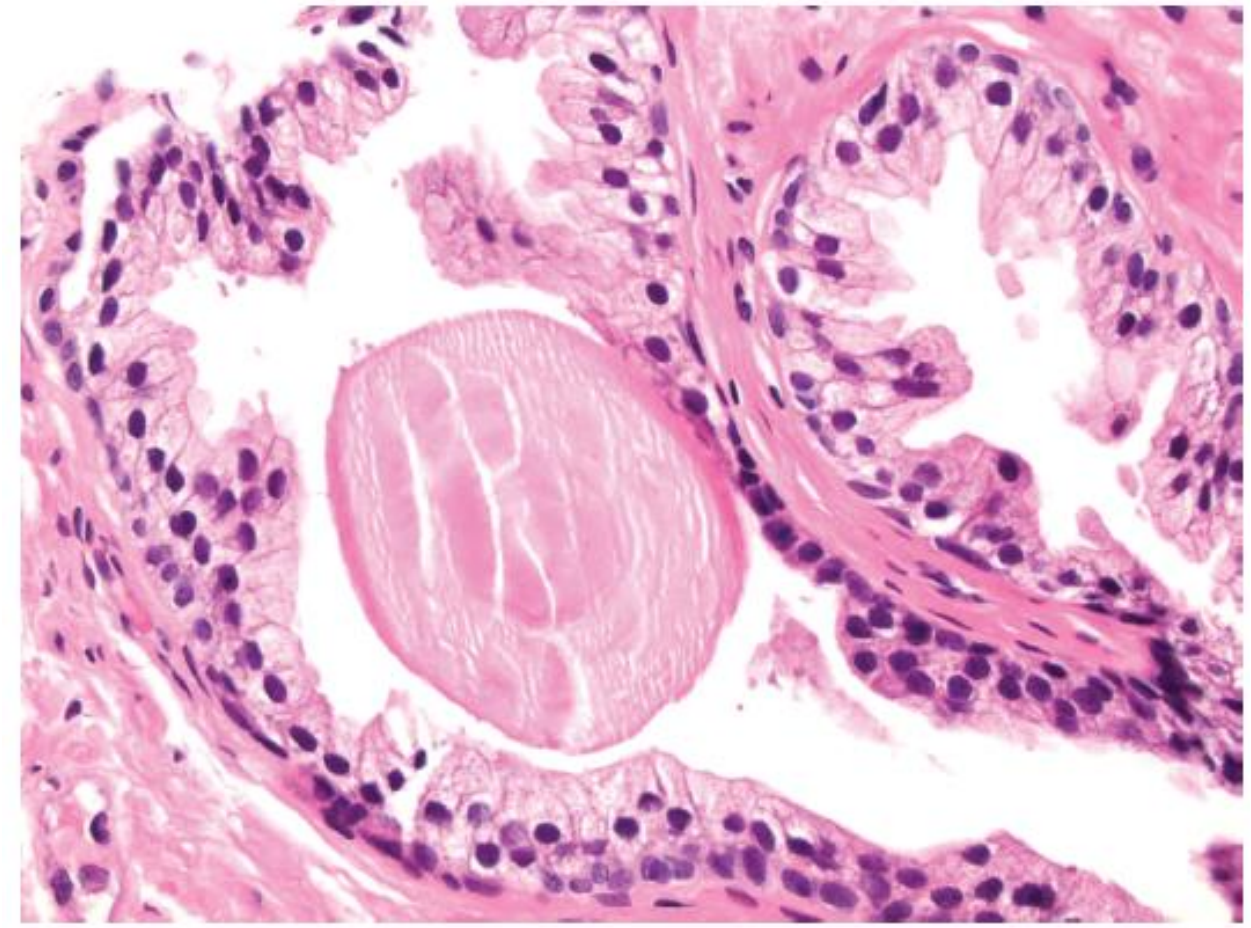


**Fig 5- Corpora amylacea is seen within the lumen**

## INCIDENCE AND EPIDEMIOLOGY

Prostate cancer is a disease which affects elderly men above 65 years of age. Prostate carcinoma is the coming under the second frequent diagnosed cancer among men across the globe and the fifth position among most reported carcinoma overall according to previous studies.[3] Restricted data available shown by studies on prostate carcinoma revealed significant differences in, incidence, preciptating factors and disease characteristics of prostate carcinoma.[3]

In India, true incidence of prostatic carcinoma is difficult to estimate due to restricted data available as it is not a reported disease and presence of few population-based cancer registries[PBCRs] among Indian population .[3]Annual Percentage Change of Karnataka is 3.4%

according to study done considering PBCR during the time period 2009-2011 in various metro cities in India .[3] Kolar studies on prostate cancer cases revealed 2.58% out of all other cancers [11,12]. Prostate carcinoma are common in developed countries like Australia, North America

This variation would be due to intensive screening for prostate carcinoma in developed countries but other factors such as lifestyle differences (diet, etc.) also to be considered important as well.

## RISK FACTORS[19,20,21,22,23,24,25,26,27,28,29,30,31,32]

1. Age: Prostate carcinoma is the most commonly seen in elderly males.
2. Ethnicity: differs among different racial groups.
3. Diet: low folate and vitamin B12, obesity, insulin and physical activity, cigarette smoking,
4. Chronic inflammation : There is a strong connection between prostate carcinoma and prostatitis
5. Sexually transmitted disease (STD): HPV & trichomonas vaginalis associated with prostate cancer.
6. Environmental carcinogens: Bisphenol A (BPA), Agent orange (AO) & Chlordecone are associated with increased risk of malignancy.

## PROTECTIVE FACTORS[33]

Diet: Dietary soy and green tea, Tomatoes and lycopene, Vitamin E, Selenium

Among which our institution follows American Urologic Association (AUA) Recommendations, in which there will be combined decision making between clinician and patient. Screening can be done for patients with age >40 yr. Discontinuation of screening can be done when the Life expectancy of the patient is <10 yr. Screening tests which can be used are PSA, digital rectal examination. Annual screening is done for patients >40 yrs.

**SCREENING FOR PROSTATIC CARCINOMA:**[33]

1. PSA
2. Digital rectal exam (DRE): it has low sensitivity and specificity. A DRE checks for the consistency, size, and texture of the prostate gland. An abnormal DRE is any nodularity, induration, or asymmetry.

**CLINICAL FEATURES:** Increased frequency, Urinary retention. hesitancy, nocturia, weight loss, impotency and hematuria noted in most of the patients[34]

**CATEGORY CRITERIA**[35,36]

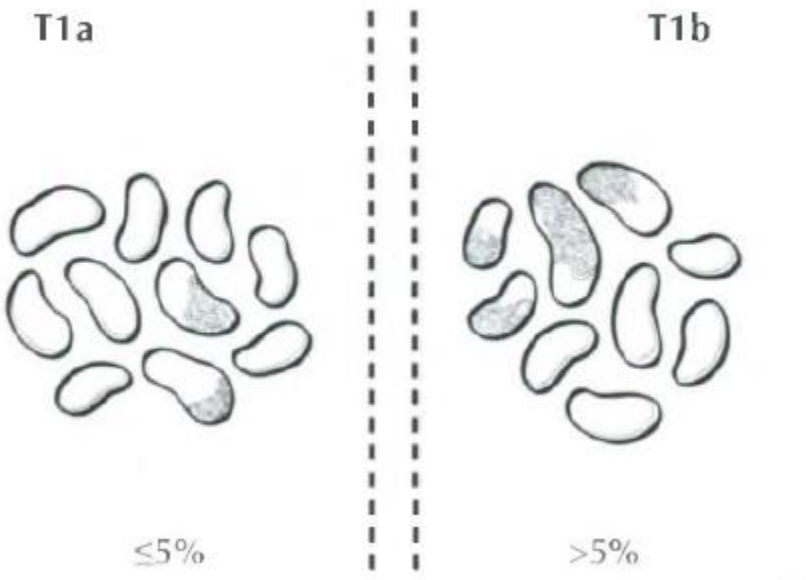



**Fig 6- Clinical stage T1a and T1b**

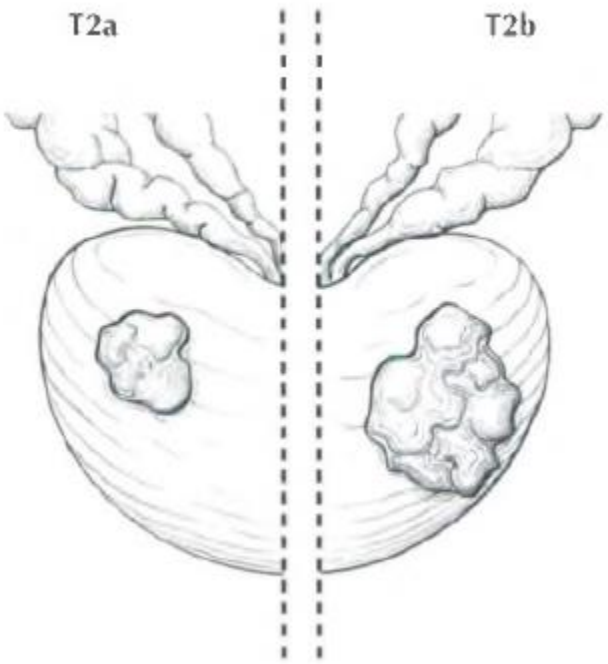



**Fig 7-Clinical stage T2a and T2b**

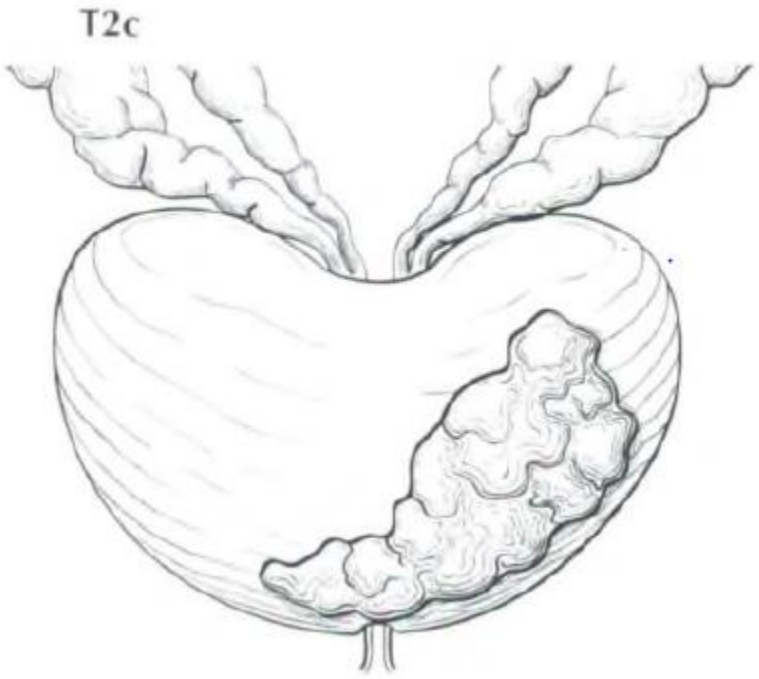



**Fig 8-Clinical stage T2c**

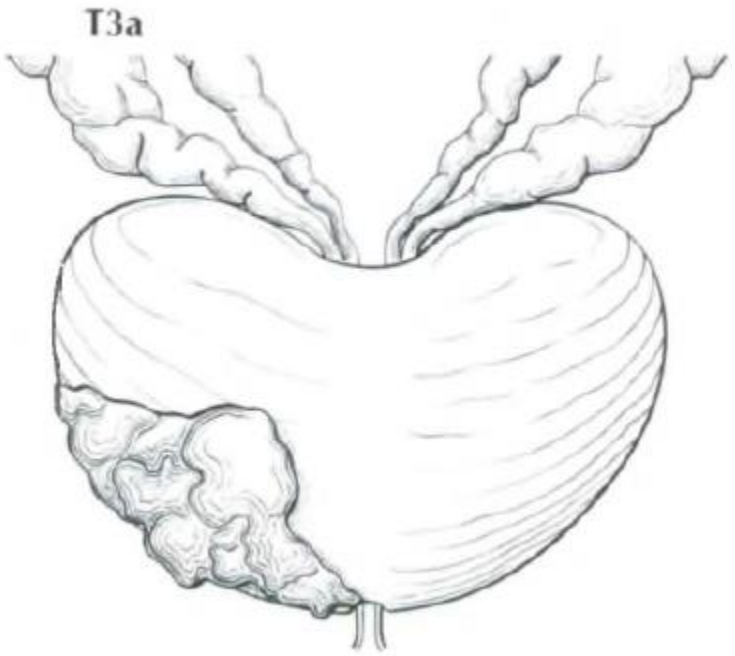



**Fig 9-Clinical and pathological stage T3a**

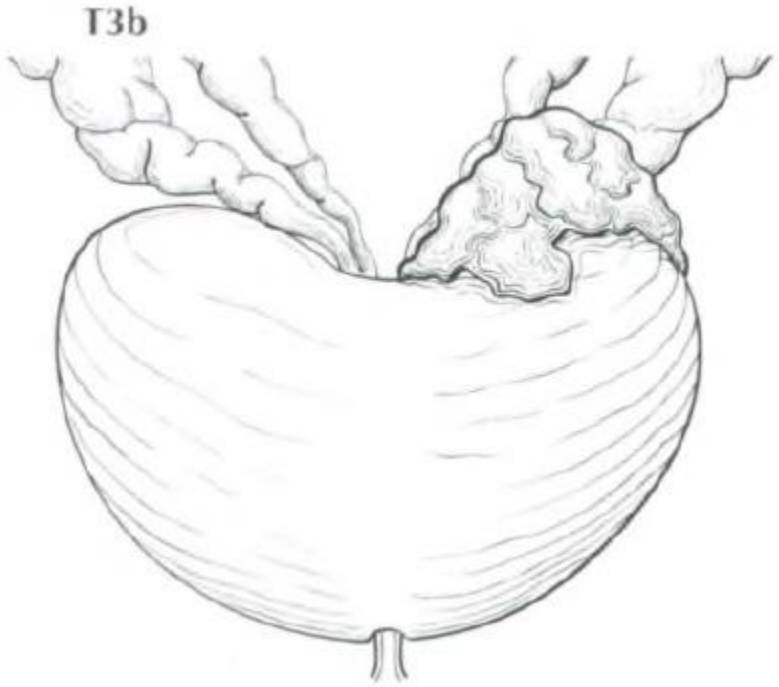



**Fig 10-Clinical and pathologic stage T3b**

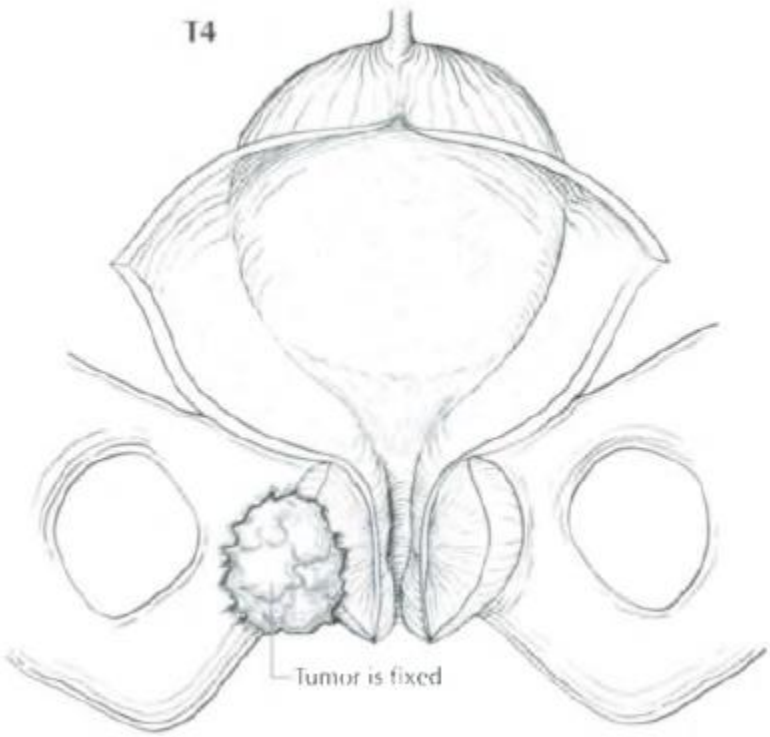



**Fig 11-Clinical and pathological stage T4**

**TABLE 1- World Health Organisation(WHO) Classification of prostate tumors 2016[37]**

**Epithelial tumours**

Glandular neoplasms

Acinar adenocarcinoma

Atrophic

Microcystic

Foamy gland

Mucinous (colloid)

Signet ring-like cell

Pleomorphic giant cell

Sarcomatoid

Prostatic intraepithelial neoplasia,

high-grade

Intraductal carcinoma

Ductal adenocarcinoma

Cribriform

Papillary

Solid

**Urothelial carcinoma**

Squamous neoplasms

Adenosquamous carcinoma

Squamous cell carcinoma

Basal cell carcinoma

**Neuroendocrine tumours**

Adenocarcinoma with neuroendocrine

Well-d ifferentiated neuroendocrine tumour

Small cell neuroendocrine carcinoma

Large cell neuroendocrine carcinoma

**Mesenchymal tumours**

Angiosarcoma

Stromal tumour of uncertain malignant potential

Stromal sarcoma

Leiomyosarcoma

Rhabdomyosarcoma

Leiomyoma

Synovial sarcoma

Inflammatory myofibroblastic tumour

Osteosarcoma

Undifferentiated pleomorphic sarcoma

Solitary fibrous tumour

Solitary fibrous tumour, malignant

Granular cell tumour

**Haematolymphoid tumours**

Diffuse large 8-cell lymphoma

Chronic lymphocytic leukaemia

Small lymphocytic lymphoma

Follicular lymphoma

Mantle cell lymphoma.

Acute myeloid leukaemia

B lymphoblastic leukaemia/lymphoma

**Miscellaneous tumours**

Pseudohyperplastic Cystadenoma

Nephroblastoma

Rhabdoid tumour

Germ cell tumours

Clear cell adenocarcinoma

Melanoma

Paraganglioma

Neuroblastoma

**Metastatic tumours**

Tumours of the seminal vesicles Solid

Epithelial tumours

Adenocarcinoma

Squamous cell carcinoma

**Mixed epithelial and stromal**

tumours Cystadenoma

**Mesenchymal tumours differentiation**

Leiomyoma

Schwannoma

Mammary-type myofibro blastoma

Gastrointestinal stromal tumour, NOS

Leiomyosarcoma

**Mesenchymal tumours**

Angiosarcoma

Liposarcoma

Solitary fibrous tumour

Haemangiopericytoma

**Miscellaneous tumours**

Choriocarcinoma

Seminoma

Wel l-differentiated neuroendocrine tumour

Lymphomas

Ewing sarcoma

## Metastatic tumors

**Table 2-STAGE GROUPING OF PROSTATE CARCINOMA[36]**

| | | | |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage 1 | T1a-2a | N0 | M0 |
| Stage 2 | T2b-c | N0 | M0 |
| Stage 3 | T3 | N0 | M0 |
| Stage 4 | T4<br>Any T<br>Any T | N0<br>N1<br>Any N | M0<br>M0<br>M1 |

**TABLE-3-AMERICAN JOINT COMMITTEE ON CANCER PROGNOSTIC STAGING OF PROSTATE CARCINOMA [36]**

| T Stage | N Stage | M Stage | PSA (ng/dL) | Grade Group | Stage Group |
|---|---|---|---|---|---|
| cT1a-c, cT2a | N0 | M0 | <10 | 1 | I |
| pT2 | N0 | M0 | <10 | 1 | I |
| cT1a-c, cT2a | N0 | M0 | ≥10, <20 | 1 | IIA |
| pT2 | N0 | M0 | ≥10, <20 | 1 | IIA |
| cT2b-c | N0 | M0 | <20 | 1 | IIA |
| T1-2 | N0 | M0 | <20 | 2 | IIB |
| T1-2 | N0 | M0 | <20 | 3 ~ 4 | IIC |
| T1-2 | N0 | M0 | ≥20 | 1 ~ 2 | IIIA |
| T1-2 | N0 | M0 | ≥20 | 3 ~ 4 | IIIA |
| T3-4 | N0 | M0 | Any | 1 ~ 4 | IIIB |
| Any T | N0 | M0 | Any | 5 | IIIC |

## BCL2 AND BAX

Apoptosis(programmed cell death) plays an important role in a variety of biological phenomena including tissue homeostasis, morphogenesis and tumorigenesis.There are two common pathways for initiation of apoptosis ie, intrinsic(mitochondrial)and extrinsic(death receptor)pathways.[38] Intrinsic pathway is regulated by proteins of Bcl2 family[39]This family consists of two main groups namely proapoptotic protein ie, Bax, Bak, Bad, Bcl-Xs, Bid, Bik, Bim, Hrk and antiapoptotic proteins ie, Bcl2,Bcl-Xl, Bcl-W, Bfl-1,Mcl-1[39].

Bcl2 is an important antiapoptotic gene encoding a protein that confers cells survival advantage by inhibiting apoptosis.[40]Its function is to preserve mitochondrial integrity , to block the release of cytochrome c and to prevent loss of mitochondrial membrane potential and cell death by interfering with the action of Bax and Bak.[40]The Bax gene is a member of Bcl2 and a transcriptional target of p53.[41]Its proapoptotic protein promotes cell death and neutralises the antiapoptotic function of Bcl2.[41]

# MATERIAL & METHODS

# MATERIALS AND METHODS

**STUDY DESIGN** – Retrospective observational study

**SOURCE OF DATA**: Transurethral resected prostatic (TURP) Chips positive for prostate carcinoma, received in the Department of Pathology,

**STUDY COURSE**- September 2020 to October 2022

**DURATION OF STUDY** – 2 years

**METHODOLOGY**

All Transurethral resected prostatic(TURP) Chips positive for carcinoma prostate confirmed by histo-pathological examination was added in the study. Data regarding the clinical details (age, Stage of the disease) was collected from Medical Record Department. H and E slides were reviewed for Histopathological types and Gleason's score of the tumor. Radiologic findings (USG,MRI or CT Findings) with respect to stage of disease, size of lesion, were noted.

TUMOR SIZE : Recent studies showed that tumor size along with other parameters like PSA and Gleason's score contributes in tumor progression and patient prognosis[42]

In this study we have divided the tumor size into 3 groups by MRI results taking the largest dimensions on MRI

| Size |
|---|
| 1-3 cm |
| >3- 6 cm |
| >6 cm |

**TABLE-4-2014 MODIFIED GLEASON GRADING AND GRADE GROUP COMPARISON FOR PROSTATE CARCINOMA[18]**

| Grade | GLEASON SCORE | HISTOLOGIC FEATURES |
|---|---|---|
| 1 | ≤3 + 3 = 6 | Only individual discrete well-formed glands |
| 2 | 3 + 4 = 7 | Predominantly well-formed glands with lesser component of poorly formed glands, fused glands, glomerations, or cribriform glands |
| 3 | 4 + 3 = 7 | Predominantly poorly formed glands, fused glands, glomerations, or cribriform glands with lesser component of well-formed glands (if >5%) |
| 4 | 4 + 4 = 8<br>3 + 5 = 8<br>5 + 3 = 8 | glands, glomerations, or cribriform glands<br>Predominantly well-formed glands with lesser component of sheets, cribriform glands with comedonecrosis, or single cells.<br>Predominantly sheets, cribriform glands with comedonecrosis, or single cells with lesser component of well-formed glands (if >5% |
| | ≥4 + 5 = 9 | Only sheets, cribriform glands with comedonecrosis, or single cells |

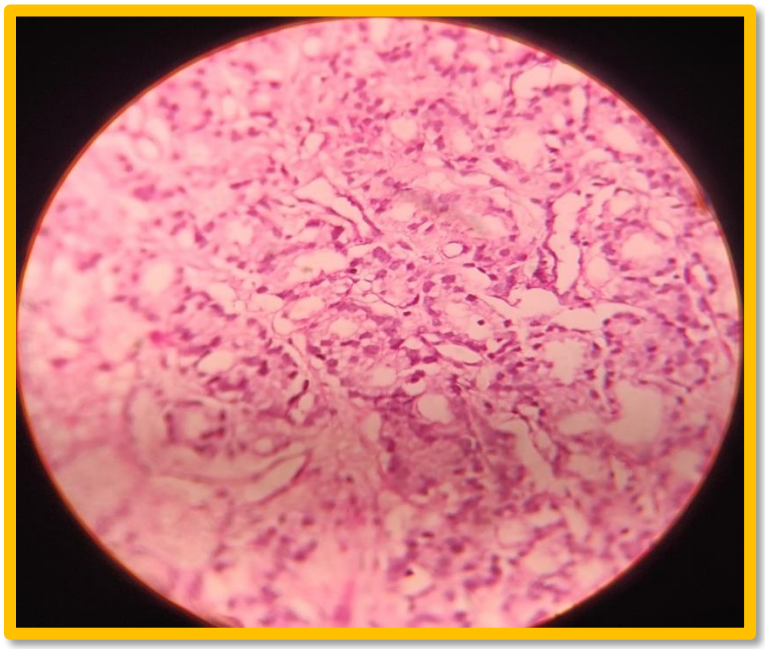


**Fig 12- Shows H and E stained slide with 100x power Gleason score -3+3=6-discrete individual glands**

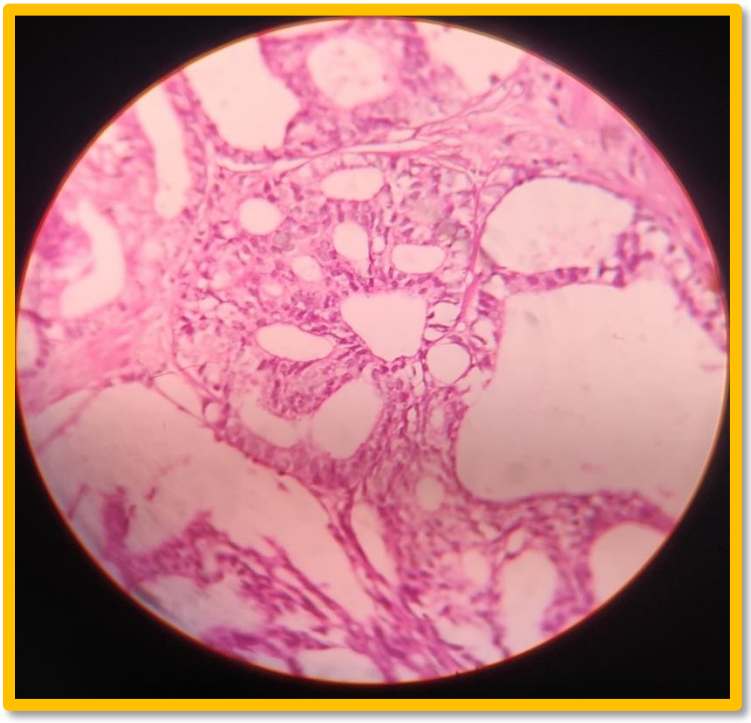


**Fig 13- Shows H and E stained slide with 100x power Gleason score-3+4=7-predominant well formed glands**

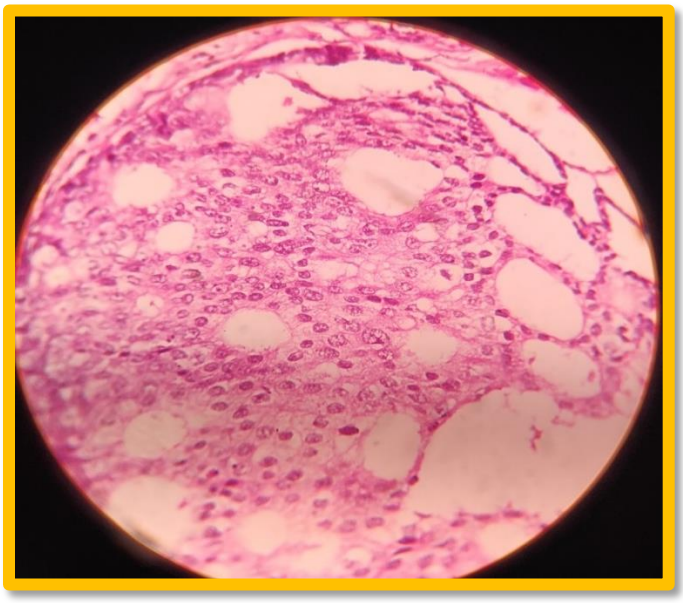


**Fig 14- Shows H and E stained slide with 100x power.Gleason score-4+3=7-predominantly poorly formed glands**

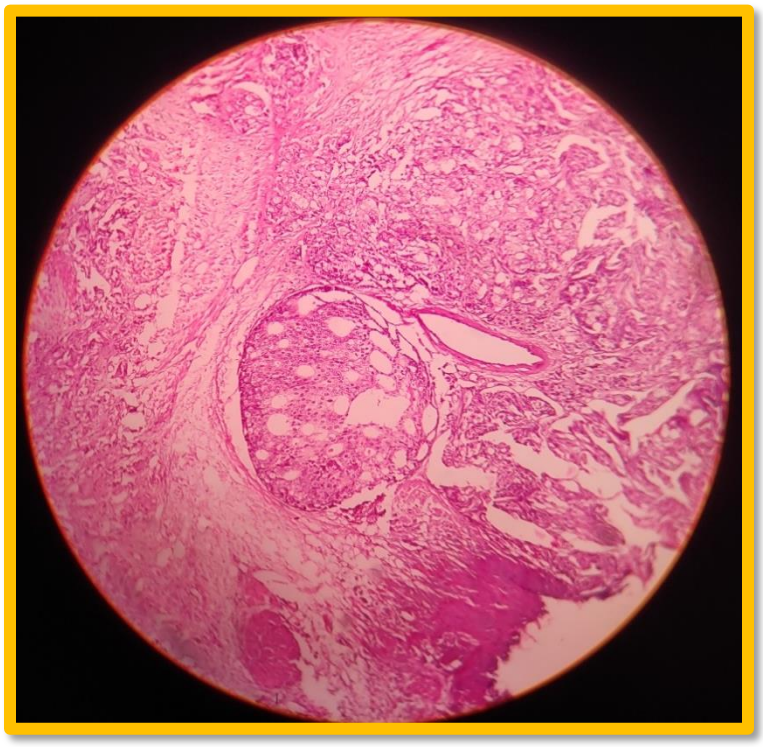


**Fig 15- Shows H and E stained slide with 40x power Gleason score-4+4=8-glands, glomerulations or cribriform**

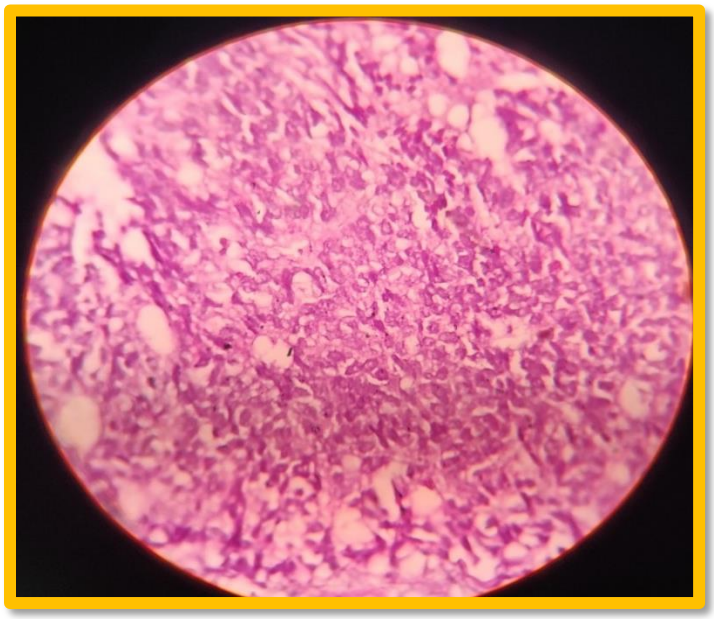


**Fig 16-**: **Shows H and E stained slide with 400x power Gleason score-5+5, tumor cells predominantly arranged in sheets.**

## IMMUNOHISTOCHEMISTRY ANTIBODY DETAILS

IHC PROTOCOL

1) Section Cutting: Sections are cut at approximately 3-4 µ m, floated on to positive charged slides and incubated at 37° C for one day and further incubated at 58° C overnight.

2) Deparaffinization and Dexylinisation

Xylene –I - 15 mins

Xylene –I I - 15 mins

Ab alcohol – I - 1min

Ab alcohol – II - 1min

90%Alcohol – 1min

70%Alcohol -1min

3) Tap water – 10 min washing

4) Distilled water – 5 min rinsing

5) Antigen Retrieval

Microwave at power 10 for 2 cycles of 6 minutes each in TRIS EDTA BUFFER of PH

9.0. Later Slides were cooled to room temperature.

6) Transfer to TBS buffer

7) Peroxidase block

8) TBS buffer

9) Power block

10) Drain and cover section with TARGET Ab

11) TBS buffer

12) Probe

13) TBS buffer

14) Super sensitive polyp –HRP

15) TBS buffer

16) DAB Color development

17) TBS buffer

18) Tap water

19) Hematoxylin Counter stain

20) Tap water

21) 90%Alcohol

22) Absolute Alcohol

23) Alcohol: Xylene 1:1

24) Xylene

25) Mount with DPX

**POSITIVE CONTROL-**Tonsil tissue was taken as a positive control

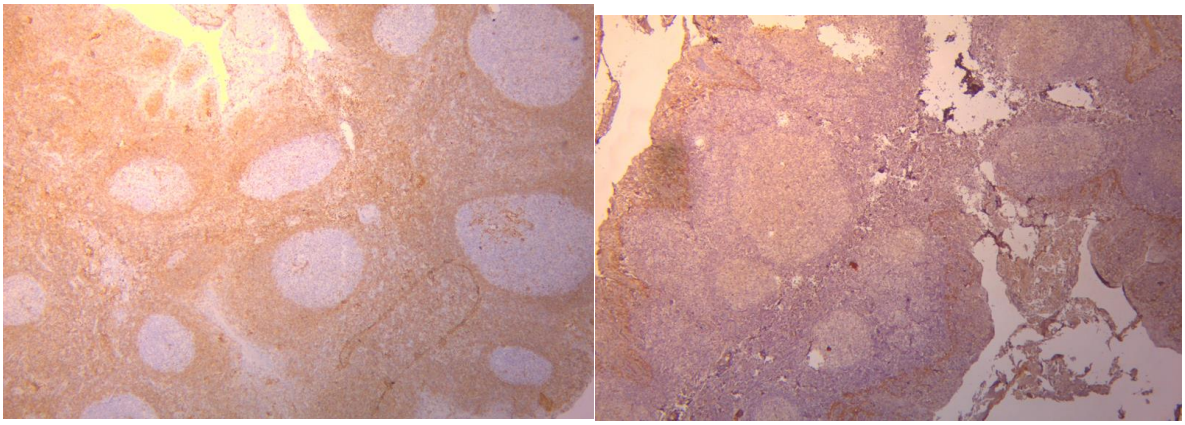


**Fig 17-Positive control for both Bcl2 and Bax gene-Tonsil**

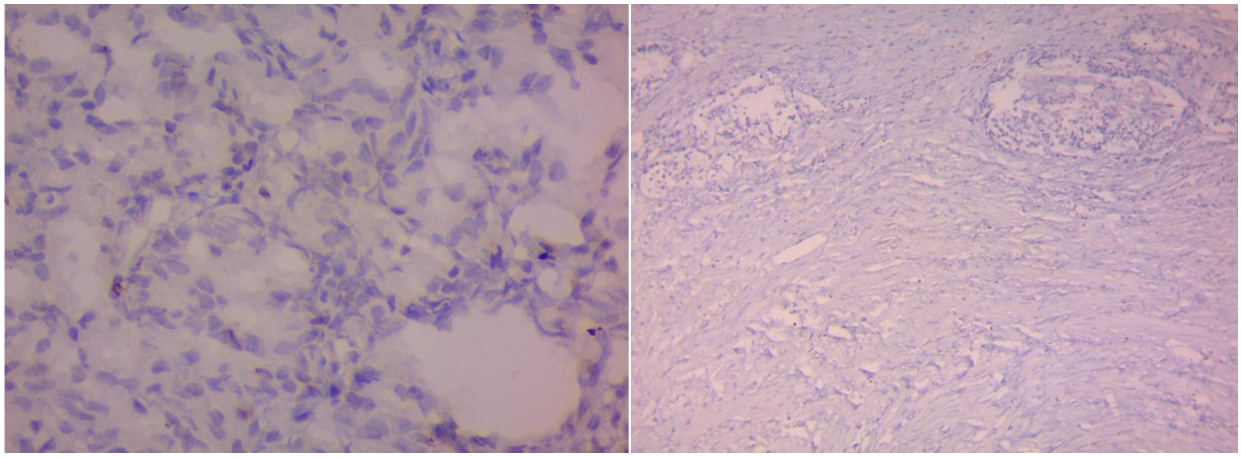


**Fig 18-IHC STAINING-BCL2 AND BAX -Score 0- negative**

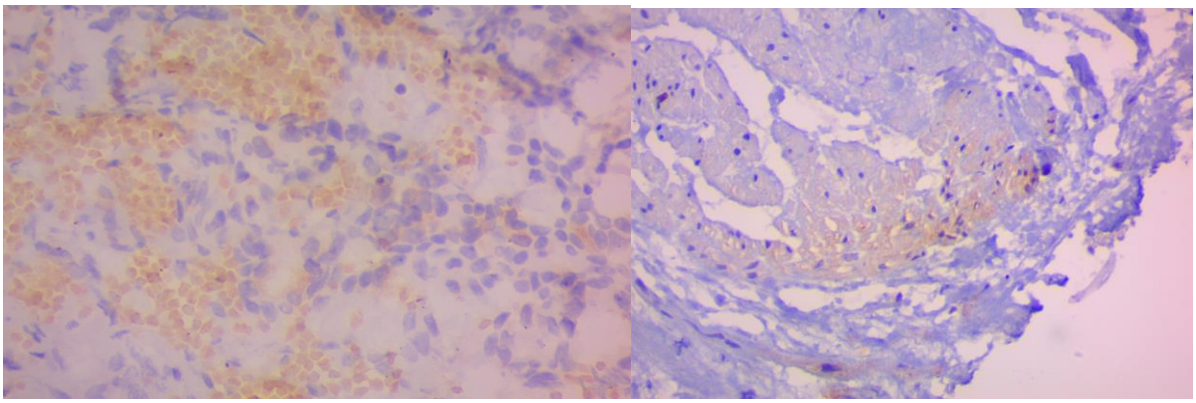


**Fig 19-IHC STAINING-BCL2 AND BAX -Score 1- faint staining**

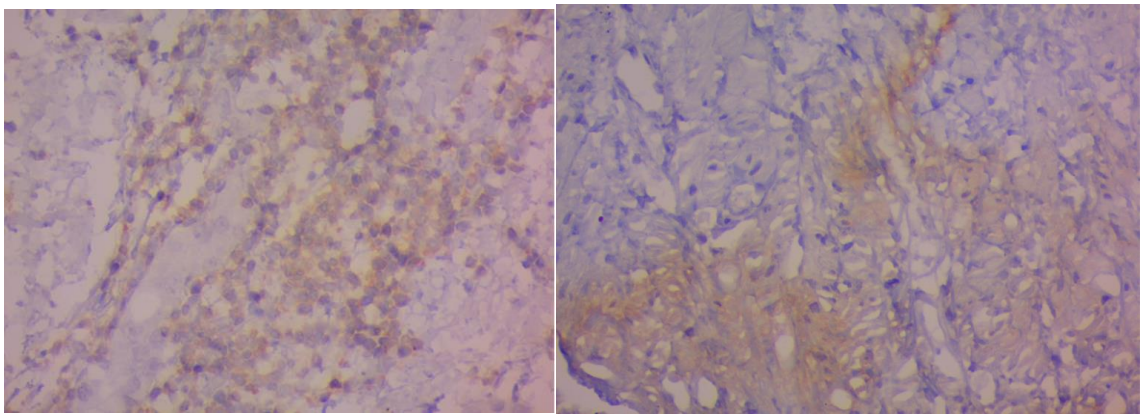


**Fig 20-IHC STAINING-BCL2 AND BAX Score 2-moderate staining**

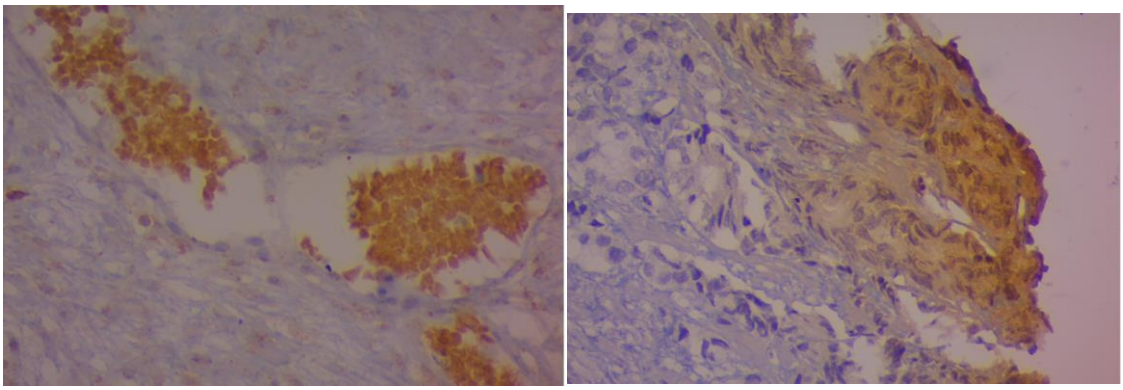


**Fig 21-IHC STAINING-BCL2 AND BAX Score 3- strong staining**

**STUDY POPULATION:-**

**INCLUSION CRITERIA:**

All prostate Adenocarcinoma cases which are diagnosed on Histopathology will be included

**EXCLUSION CRITERIA:**

- Patients diagnosed with metastatic adenocarcinoma of prostate
- Patients subjected to radiotherapy and chemotherapy.
- Recurrent lesion of prostate.

## IMMUNOSTAINING FOR Bax AND Bcl2 [39]

Multiple 4 micrometer thick sections of formalin fixed, paraffin embedded tissues are cut for immunohistochemical studies.

A polymer based (EnVision™) immunohistochemical method is used for detection of Bax and Bcl2. Reactive lymph node with follicular hyperplasia is used for positive control.Immunostaining without adding antibody is used as negative control. Immunostained sections are examined by under 40X objective and 10X eyepiece under light microscope.Bax and Bcl2 staining is cytoplasmic.

Protein expression is scored as :

1.Mild: faint cytoplasmic stain.

2.Moderate: diffuse cytoplasmic stain.

3. Strong; diffuse intense cytoplasmic stain.

Proportion of malignant cells which has positive staining is considered in reporting.Immunostaining is quantified as H-score which considers both intensity and percentage of cells stained in each intensity. H-score was calculated as follows:

(% of cells stained at intensity 1 x 1) +(% of cells stained at intensity 2 x 2)+ (%of cells stained at intensity 3 x 3).

H- score between 0 and 300, in which 300 is equal to 100% of tumor cells stained strongly.

H- score above 50 , will be considered to be positive for Bax and Bcl2 expression.

All the scoring was done by two pathologists independently & both were unaware of clinical data. All the decision were taken by both the pathologist based on the consensus. In case of any discrepancies the case was referred to a third pathologist for final decision which was acceptable to both.

## SAMPLE SIZE:

Sample size was estimated by using the proportion of Bax expression(p=97.3) in prostate cancers, alpha error is 5%, by using the formula :-

Equation sample size is = $Z_{1-\alpha}^2 p(1-p)/d^2$

Here $Z_{1-\alpha}$ = Standard normal variant

P = Expected proportion in population based on previous studies

d = absolute error of 5%

P= 97.3

q = 74

d = 5

Using the above values at 95% Confidence level a sample size of 50 subjects with prostate cancer will be included in the study.

## DATA ANALYSIS:

. Data was entered in MS excel 2007 and data was analysed using IBM SPSS(Statistical Package for the Social Sciences).Continuous data were expressed as mean and standard deviation. Appropriate statistical tests were applied, (chi-square test and Yates correction when At least 20% of expected frequencies are less than 5) and < 0.05 p values considered as significant. Pearson's correlation was done between Gleason score with Box/Bcl-2.

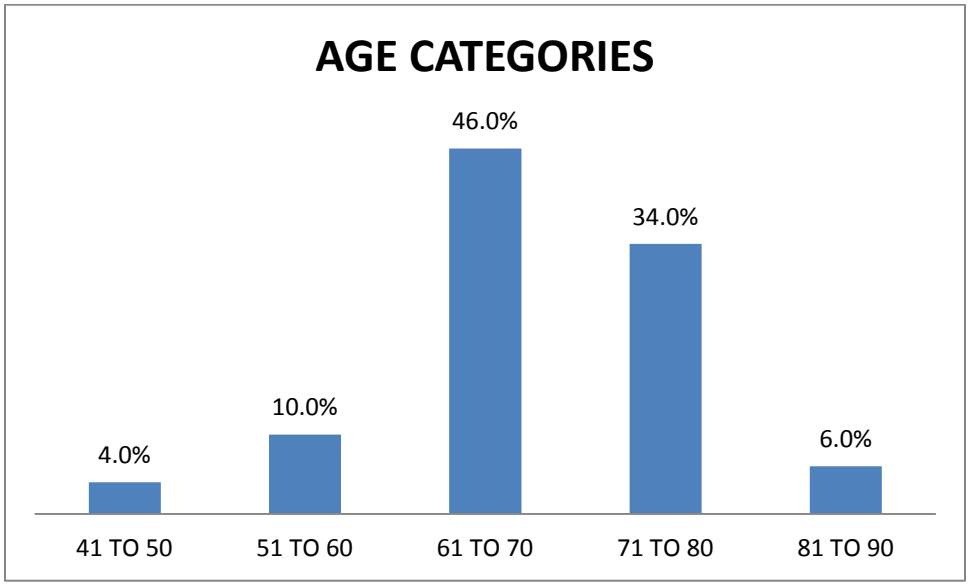
# RESULTS

## RESULTS

### TABLE NO. 5 AGE CATEGORIES

| AGE CATEGORIES | Frequency | Percentage (%) |
|---|---|---|
| 41 TO 50 | 2 | 4.0% |
| 51 TO 60 | 5 | 10.0% |
| **61 TO 70** | **23** | **46.0%** |
| **71 TO 80** | **17** | **34.0%** |
| 81 TO 90 | 3 | 6.0% |
| Total | 50 | 100.0% |

### CHART NO. 1 AGE CATEGORIES

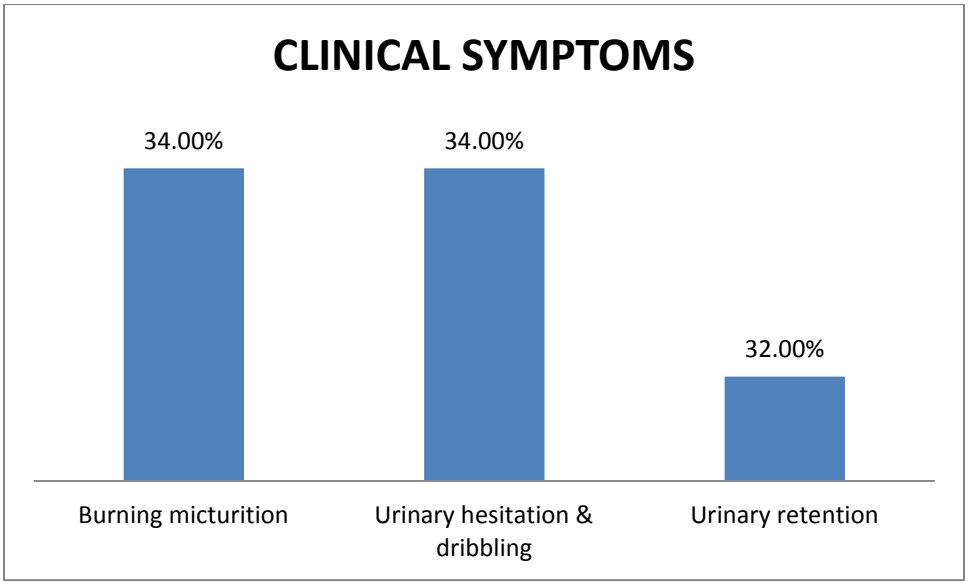



In present study majority of the study population is in 61 to 70 years age group (46%), followed by 71 to 80 years (34%).

## TABLE NO. 6-CLINICAL SYMPTOMS

| CLINICAL SYMPTOMS | Frequency | Percentage (%) |
|---|---|---|
| Burning micturition | 17 | 34.0% |
| Urinary hesitation & dribbling | 17 | 34.0% |
| Urinary retention | 16 | 32.0% |
| Total | 50 | 100.0% |

## CHART NO. 2 CLINICAL SYMPTOMS

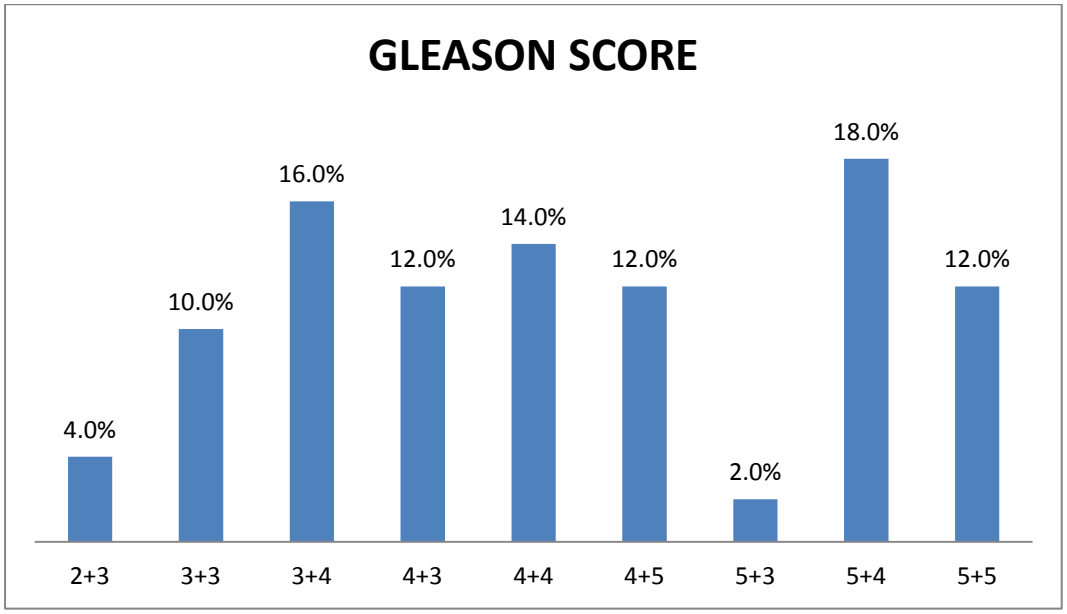



Burning micturition (34%) Urinary hesitation & dribbling (34%) were common followed by Urinary retention (32%) among urinary symptoms in present study.

## TABLE NO. 8-GLEASON SCORE

| GLEASON SCORE | Frequency | Percentage (%) |
|---|---|---|
| 2+3 | 2 | 4.0% |
| 3+3 | 5 | 10.0% |
| 3+4 | 8 | 16.0% |
| 4+3 | 6 | 12.0% |
| **4+4** | **7** | **14.0%** |
| 4+5 | 6 | 12.0% |
| 5+3 | 1 | 2.0% |
| **5+4** | **9** | **18.0%** |
| 5+5 | 6 | 12.0% |
| Total | 50 | 100.0% |

## CHART NO. 3 GLEASON SCORE

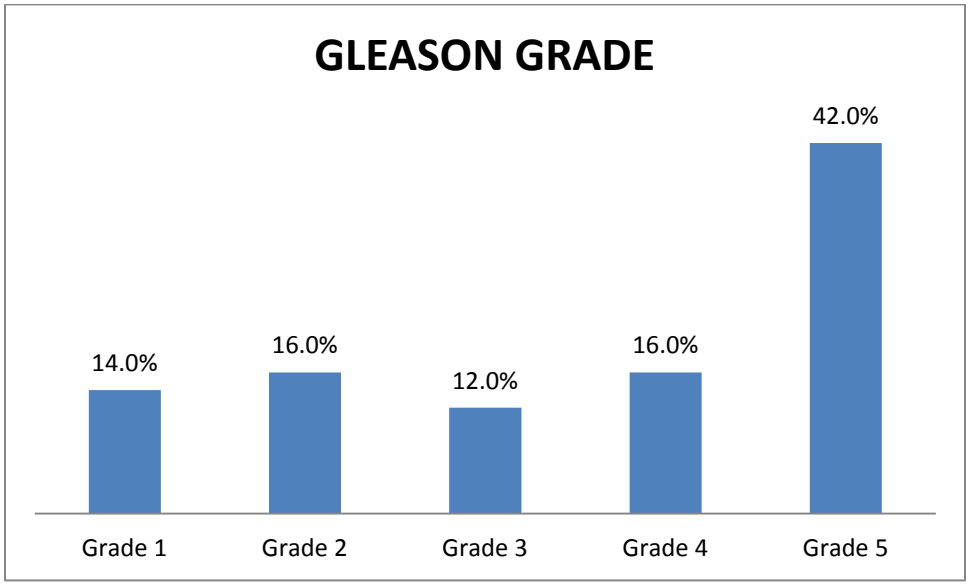



Gleason Score of 5+4 (18%) followed by 4+4 (14%) were common among present study population.

**TABLE NO. 9-GLEASON GRADE**

| GLEASON GRADE | Frequency | Percentage (%) |
|---|---|---|
| Grade 1 | 7 | 14.0% |
| **Grade 2** | **8** | **16.0%** |
| Grade 3 | 6 | 12.0% |
| **Grade 4** | **8** | **16.0%** |
| **Grade 5** | **21** | **42.0%** |
| Total | 50 | 100.0% |

**CHART NO. 4 GLEASON GRADE**

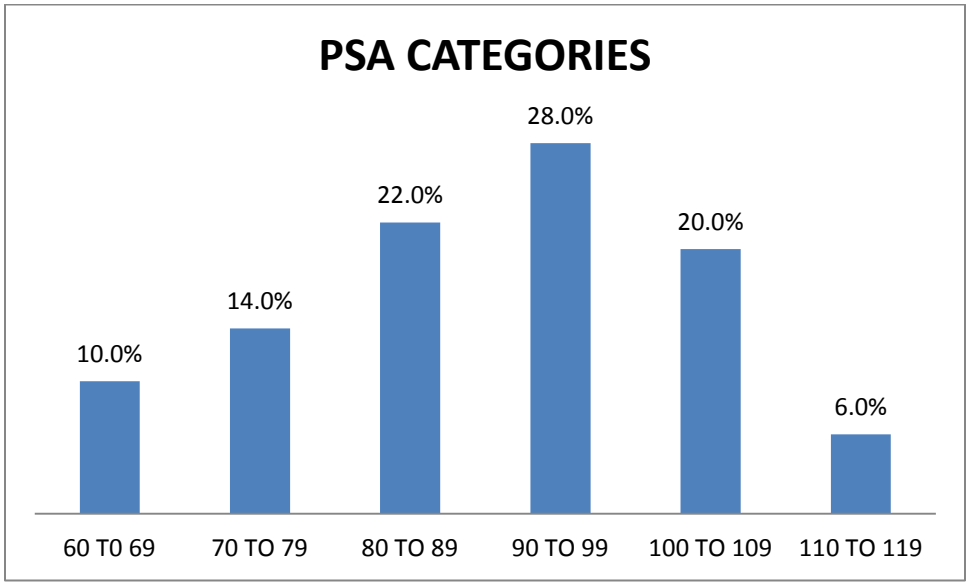



In present study majority of the study population is in Gleason grade 5(42%), followed by Gleason grade 4& 2 (16%).

**TABLE NO. 10- PSA CATEGORIES**

| PSA CATEGORIES | Frequency | Percentage (%) |
|---|---|---|
| 60 T0 69 ng/ml | 5 | 10.0% |
| 70 TO 79 ng/ml | 7 | 14.0% |
| **80 TO 89 ng/ml** | **11** | **22.0%** |
| **90 TO 99 ng/ml** | **14** | **28.0%** |
| 100 TO 109 ng/ml | 10 | 20.0% |
| 110 TO 119 ng/ml | 3 | 6.0% |
| Total | 50 | 100.0% |

**CHART NO. 5 PSA CATEGORIES**

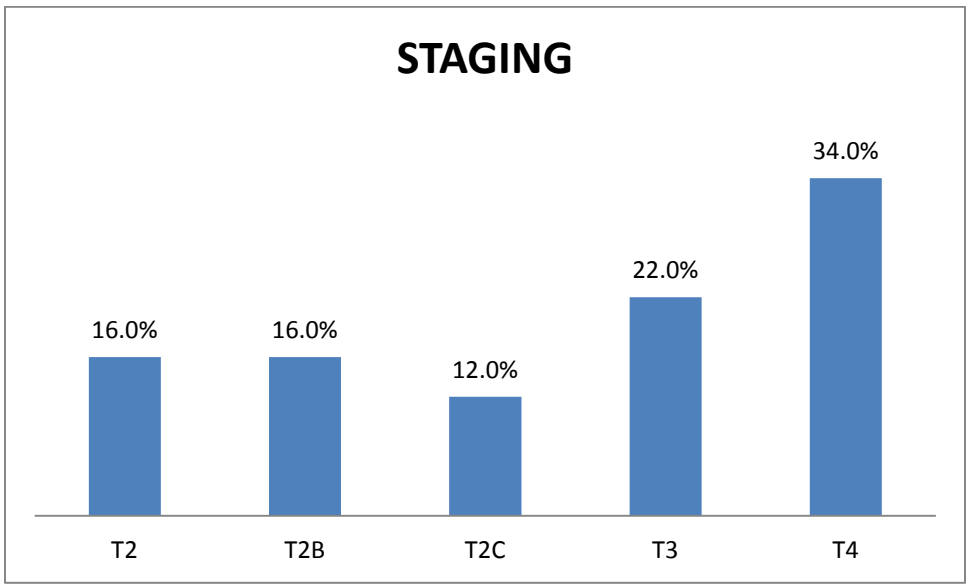



In present study majority of the study population is 90 to 99 levels of PSA (28%), followed by Gleason 80 TO 89 (22%).

**TABLE NO. 11-TUMOR STAGING CATEGORIES**

| STAGING | Frequency | Percentage (%) |
|---|---|---|
| T2 | 8 | 16.0% |
| T2B | 8 | 16.0% |
| T2C | 6 | 12.0% |
| **T3** | **11** | **22.0%** |
| **T4** | **17** | **34.0%** |
| Total | 50 | 100.0% |

**CHART NO. 6 TUMOR STAGING CATEGORIES**

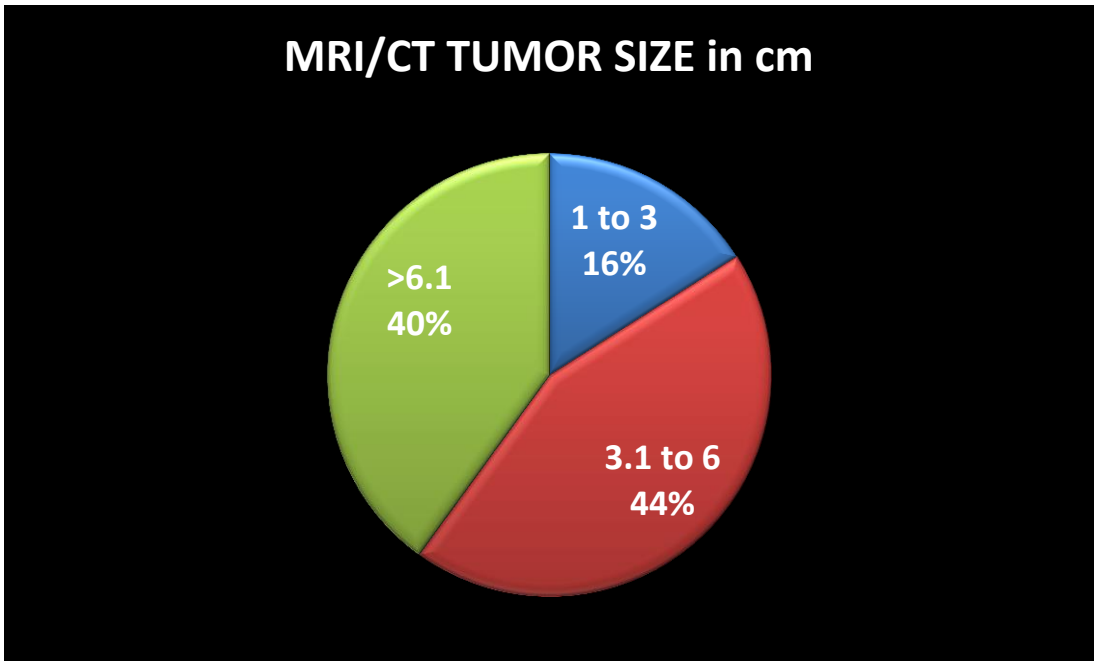



In present study majority of the study population is T4 staging (34%), followed by T3 staging (22%).

**TABLE NO. 12 TUMOR STAGING CATEGORIES**

| MRI/CT TUMOR SIZE in cm | Frequency | Percentage (%) |
|---|---|---|
| 1 to 3 | 8 | 16.0% |
| **3.1 to 6** | **22** | **44.0%** |
| **>6.1** | **20** | **40.0%** |
| Total | 50 | 100.0% |

**CHART NO. 7 TUMOR STAGING CATEGORIES**

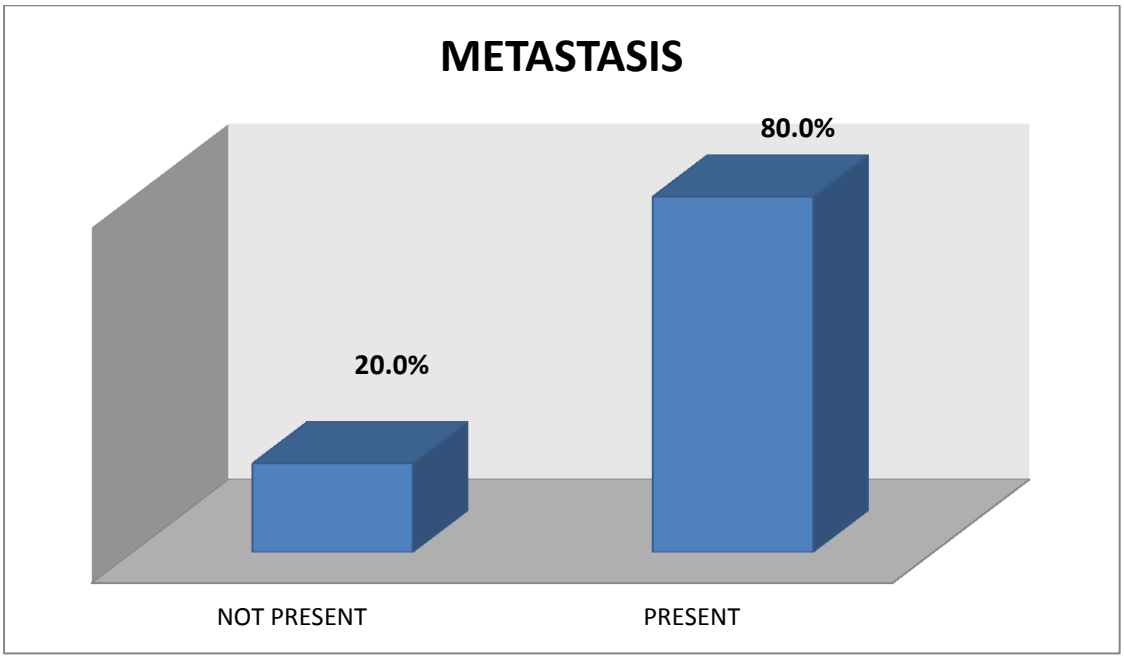



In present study majority of the study population had a tumor size of 3.1 to 6 cm (44%) followed by >6.1 cm (40%).

## TABLE NO. 13- METASTASIS

| METASTASIS | Frequency | Percentage (%) |
|---|---|---|
| NOT PRESENT | 10 | 20.0% |
| PRESENT | 40 | 80.0% |
| Total | 50 | 100.0% |

## CHART NO. 8 METASTASIS

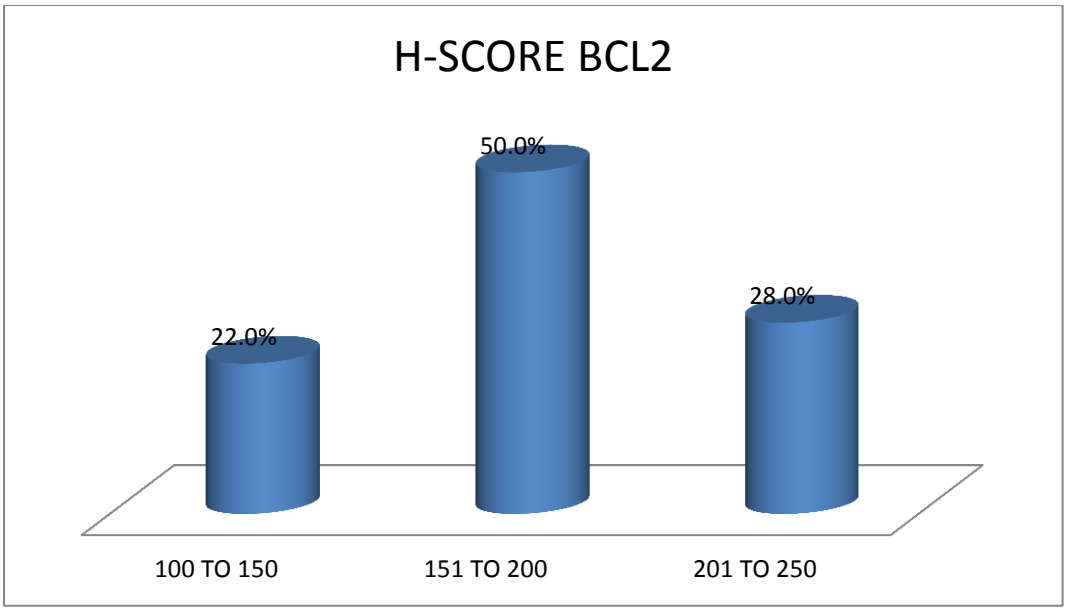



In present study majority of the study population had metastasis (80%).

## TABLE NO.14- H-SCORE BCL2

| H-SCORE BCL2 | Frequency | Percentage (%) |
|---|---|---|
| 100 TO 150 | 11 | 22.0% |
| **151 TO 200** | **25** | **50.0%** |
| 201 TO 250 | 14 | 28.0% |
| Total | 50 | 100.0% |

## CHART NO.9 H-SCORE BCL2

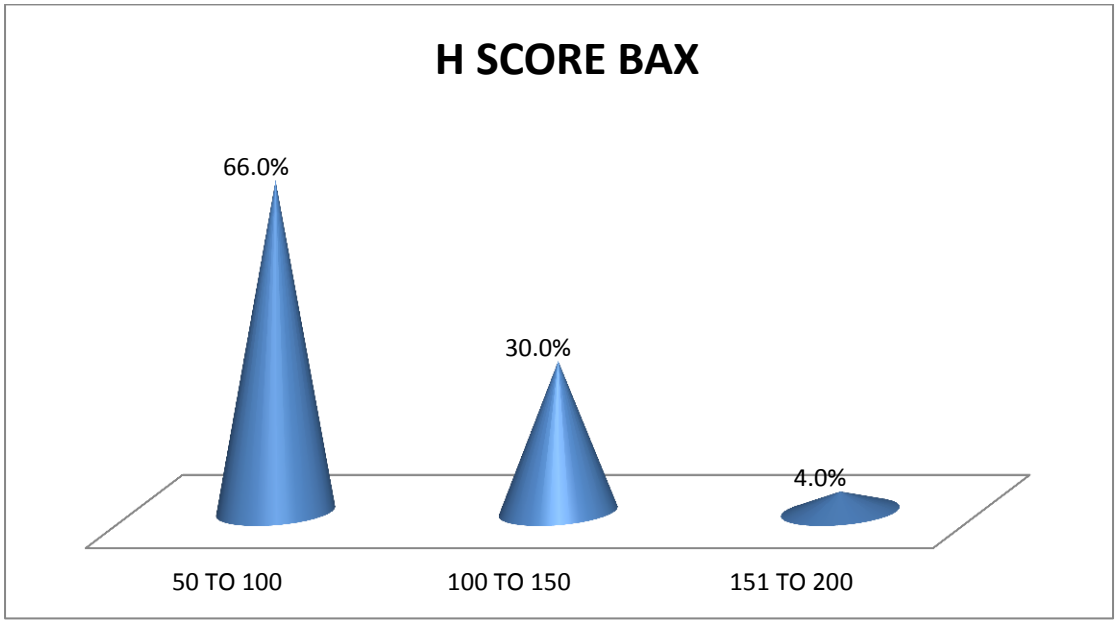



In present study majority of the study population had H-SCORE BCL2 of 151 TO 200 (50%) followed by 201 TO 250 (28%).

## TABLE NO.15- H SCORE BAX

| H SCORE BAX | Frequency | Percentage (%) |
|---|---|---|
| **50 TO 100** | **33** | **66.0%** |
| 100 TO 150 | 15 | 30.0% |
| 151 TO 200 | 2 | 4.0% |
| Total | 50 | 100.0% |

## CHART NO.10 H SCORE BAX

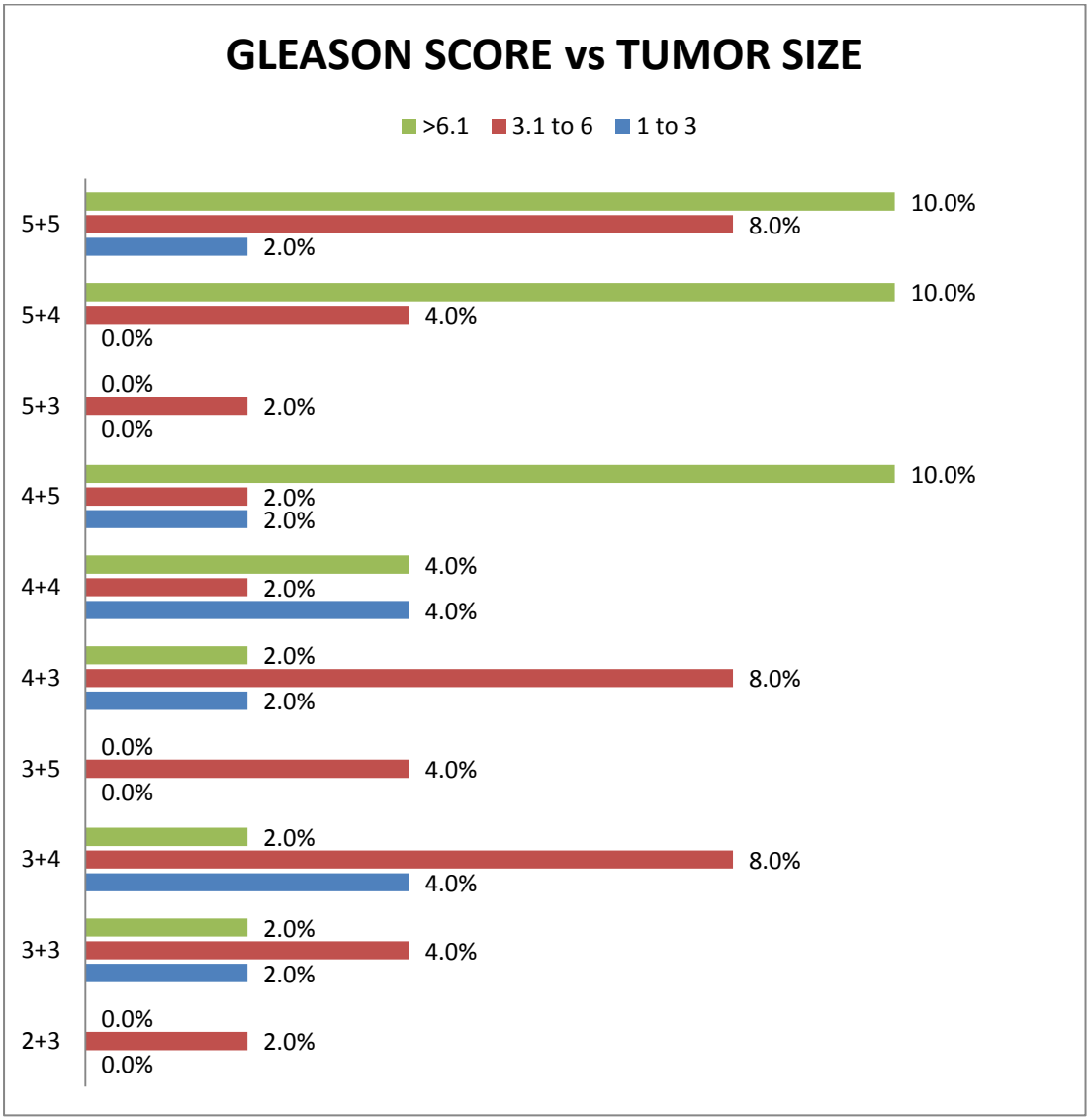



In present study majority of the study population had H-SCORE BAX of 50 TO 100 (66%) followed by 100 TO 150 (30%).

## TABLE NO.16 H SCORE BAX VS GLEASON SCORE

| GLEASON SCORE | MRI/CT TUMOR SIZE | | | | | |
|---|---|---|---|---|---|---|
| | 1 to 3 | | 3.1 to 6 | | >6.1 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| 2+3 | 0 | 0.0% | 1 | 2.0% | 0 | 0.0% |
| 3+3 | 1 | 2.0% | 2 | 4.0% | 1 | 2.0% |
| 3+4 | 2 | 4.0% | 4 | 8.0% | 1 | 2.0% |
| 3+5 | 0 | 0.0% | 2 | 4.0% | 0 | 0.0% |
| 4+3 | 1 | 2.0% | 4 | 8.0% | 1 | 2.0% |
| 4+4 | 2 | 4.0% | 1 | 2.0% | 2 | 4.0% |
| 4+5 | 1 | 2.0% | 1 | 2.0% | 5 | 10.0% |
| 5+3 | 0 | 0.0% | 1 | 2.0% | 0 | 0.0% |
| 5+4 | 0 | 0.0% | 2 | 4.0% | 5 | 10.0% |
| 5+5 | 1 | 2.0% | 4 | 8.0% | 5 | 10.0% |
| Total | 8 | 16.0% | 22 | 44.0% | 20 | 40.0% |
| P value 0.4 | | | | | | |

## CHART NO.11 H SCORE BAX VS GLEASON SCORE

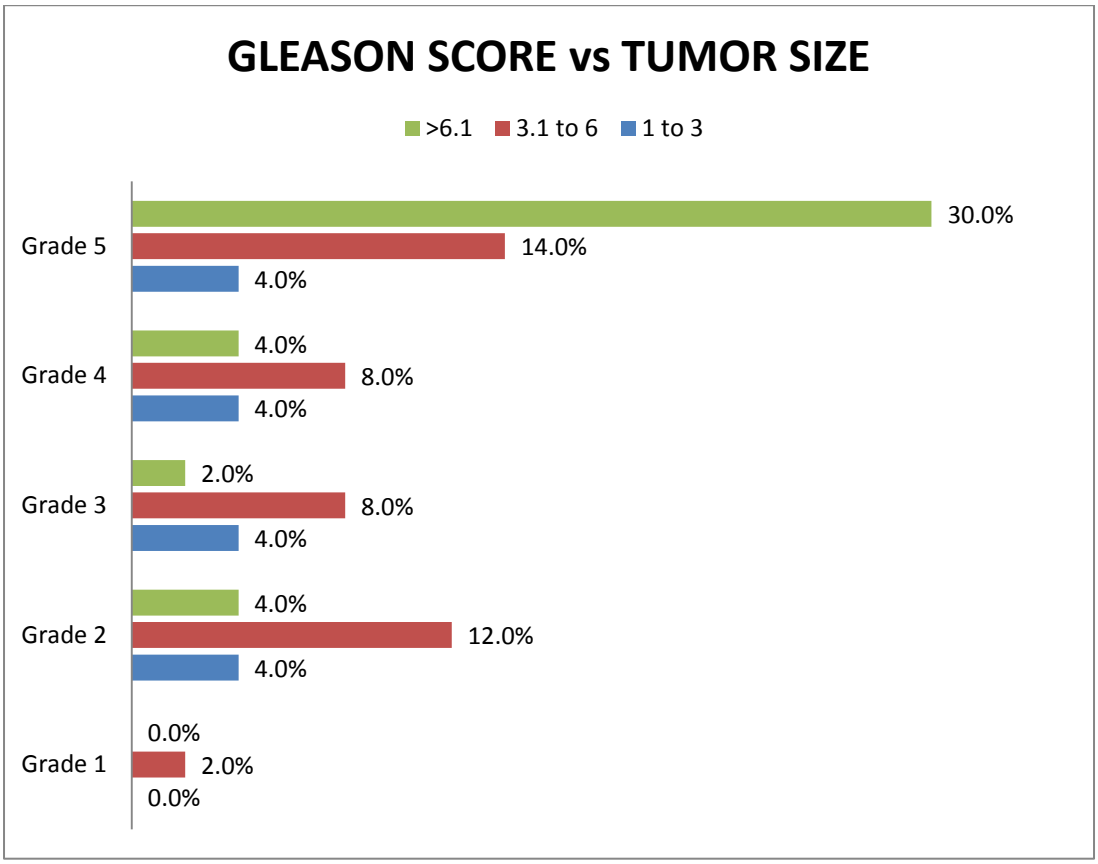



In present study Gleason score showed no significant correlation with the tumor size.

## TABLE NO.18- H SCORE BAX VS GLEASON GRADE

| GLEASON GRADE | MRI/CT TUMOR SIZE | | | | | |
|---|---|---|---|---|---|---|
| | 1 to 3 | | 3.1 to 6 | | >6.1 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| Grade 1 | 0 | 0.0% | 1 | 2.0% | 0 | 0.0% |
| Grade 2 | 2 | 4.0% | 6 | 12.0% | 2 | 4.0% |
| Grade 3 | 2 | 4.0% | 4 | 8.0% | 1 | 2.0% |
| Grade 4 | 2 | 4.0% | 4 | 8.0% | 2 | 4.0% |
| **Grade 5** | **2** | **4.0%** | **7** | **14.0%** | **15** | **30.0%** |
| Total | 8 | 16.0% | 22 | 44.0% | 20 | 40.0% |
| P value 0.1 | | | | | | |

## CHART NO.12 H SCORE BAX VS GLEASON GRADE

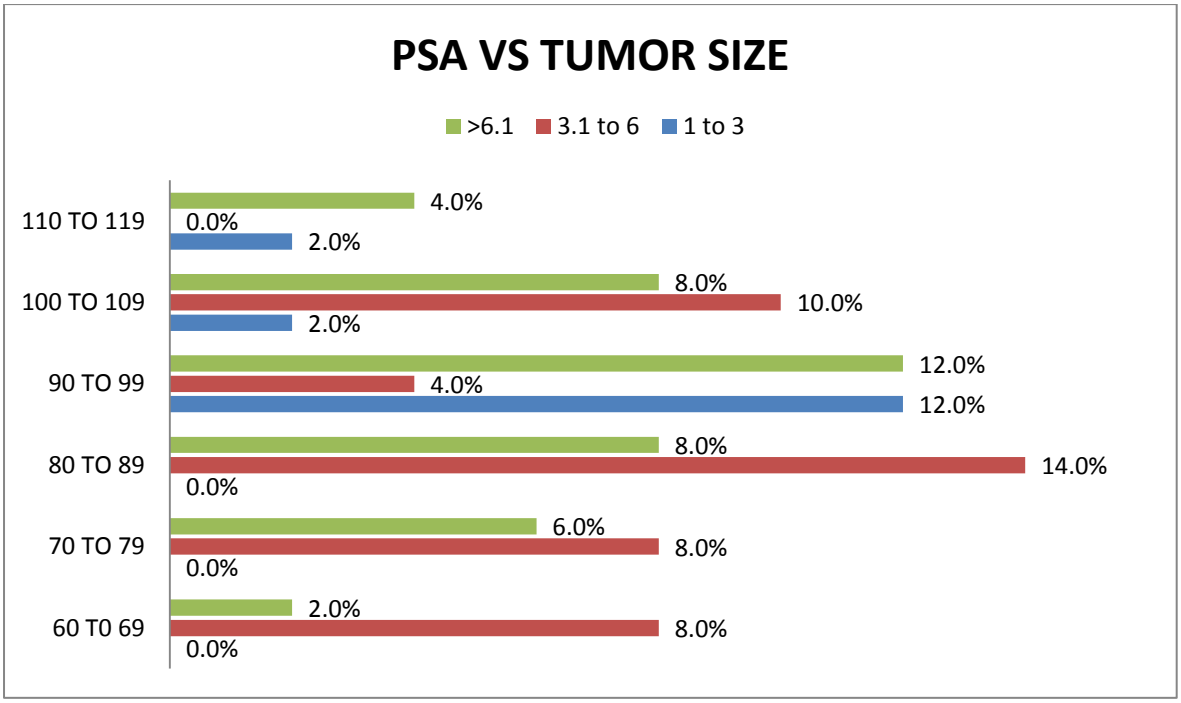



In present study Gleason grade 5 had more cases with >6.1 cm tumor size but the difference was no found to be significant showed no significant correlation with the tumor size.

## TABLE NO.19- TUMOR SIZE VS PSA

| PSA CATEGORIES | MRI/CT TUMOR SIZE | | | | | |
|---|---|---|---|---|---|---|
| | 1 to 3 | | 3.1 to 6 | | >6.1 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| 60 T0 69 | 0 | 0.0% | 4 | 8.0% | 1 | 2.0% |
| 70 TO 79 | 0 | 0.0% | 4 | 8.0% | 3 | 6.0% |
| 80 TO 89 | 0 | 0.0% | 7 | 14.0% | 4 | 8.0% |
| **90 TO 99** | **6** | **12.0%** | **2** | **4.0%** | **6** | **12.0%** |
| 100 TO 109 | 1 | 2.0% | 5 | 10.0% | 4 | 8.0% |
| 110 TO 119 | 1 | 2.0% | 0 | 0.0% | 2 | 4.0% |
| Total | 8 | 16.0% | 22 | 44.0% | 20 | 40.0% |
| P VALUE 0.04 | | | | | | |

## CHART NO.13 TUMOR SIZE VS PSA

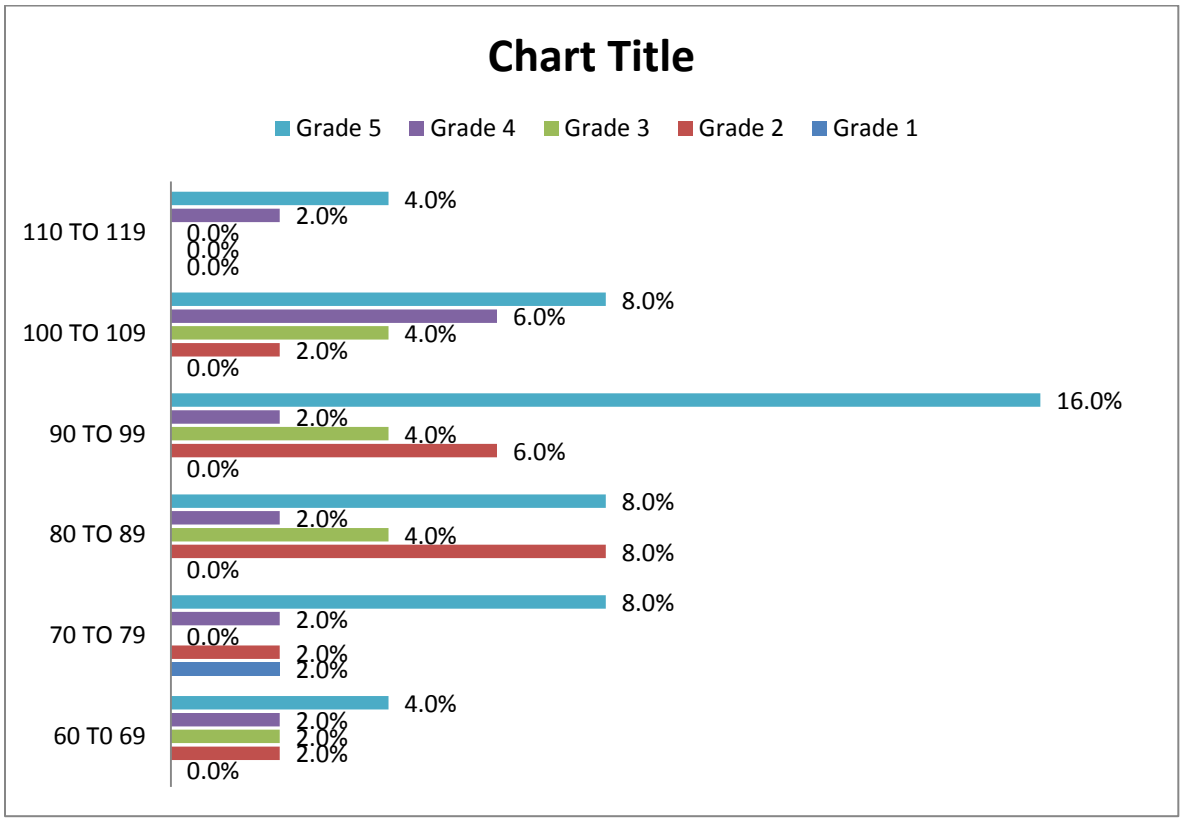



In present study PSA score grading showed no significant correlation with the tumor size.

## TABLE NO.20 PSA VS GLEASON GRADE

| GLEASON GRADE | PSA CATEGORIES | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 60 T0 69 | | 70 TO 79 | | 80 TO 89 | | 90 TO 99 | | 100 TO 109 | | 110 TO 119 | |
| | Count | N % | Count | N % | Count | N % | Count | N % | Count | N % | Count | N % |
| Grade 1 | 0 | 0.0% | 1 | 2.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0 % |
| Grade 2 | 1 | 2.0% | 1 | 2.0% | 4 | 8.0% | 3 | 6.0% | 1 | 2.0% | 0 | 0.0 % |
| Grade 3 | 1 | 2.0% | 0 | 0.0% | 2 | 4.0% | 2 | 4.0% | 2 | 4.0% | 0 | 0.0 % |
| Grade 4 | 1 | 2.0% | 1 | 2.0% | 1 | 2.0% | 1 | 2.0% | 3 | 6.0% | 1 | 2.0 % |
| Grade 5 | 2 | 4.0% | 4 | 8.0% | 4 | 8.0% | 8 | 16.0 % | 4 | 8.0% | 2 | 4.0 % |
| Total | 5 | 10.0 % | 7 | 14.0 % | 11 | 22.0 % | 14 | 28.0 % | 10 | 20.0 % | 3 | 6.0 % |
| P VALUE 0.7 | | | | | | | | | | | | |

## FIGURE NO.14 PSA VS GLEASON GRADE

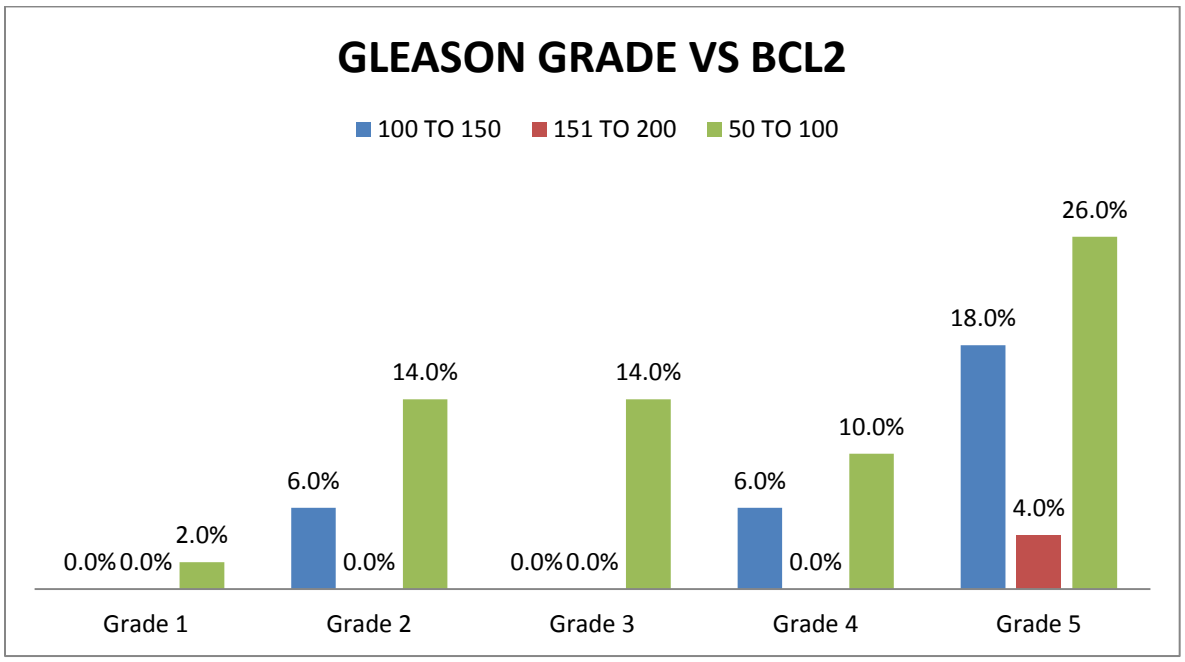



In present study Gleason grading showed no significant correlation with the tumor size

**TABLE N0 21- H-SCORE BCL2 VS GLEASON GRADE**

| GLEASON GRADE | H-SCORE BCL2 | | | | | |
|---|---|---|---|---|---|---|
| | 100 TO 150 | | 151 TO 200 | | 201 TO 250 | |
| | Count | N % | Count | N % | Count | N % |
| Grade 1 | 0 | 0.0% | 1 | 2.0% | 0 | 0.0% |
| Grade 2 | 3 | 6.0% | 6 | 12.0% | 1 | 2.0% |
| Grade 3 | 4 | 8.0% | 3 | 6.0% | 0 | 0.0% |
| Grade 4 | 2 | 4.0% | 4 | 8.0% | 2 | 4.0% |
| Grade 5 | **2** | **4.0%** | **11** | **22.0%** | **11** | **22.0%** |
| Total | 11 | 22.0% | 25 | 50.0% | 14 | 28.0% |
| P VALUE 0.09 | | | | | | |

**CHART NO-15 H-SCORE BCL2 VS GLEASON GRADE**

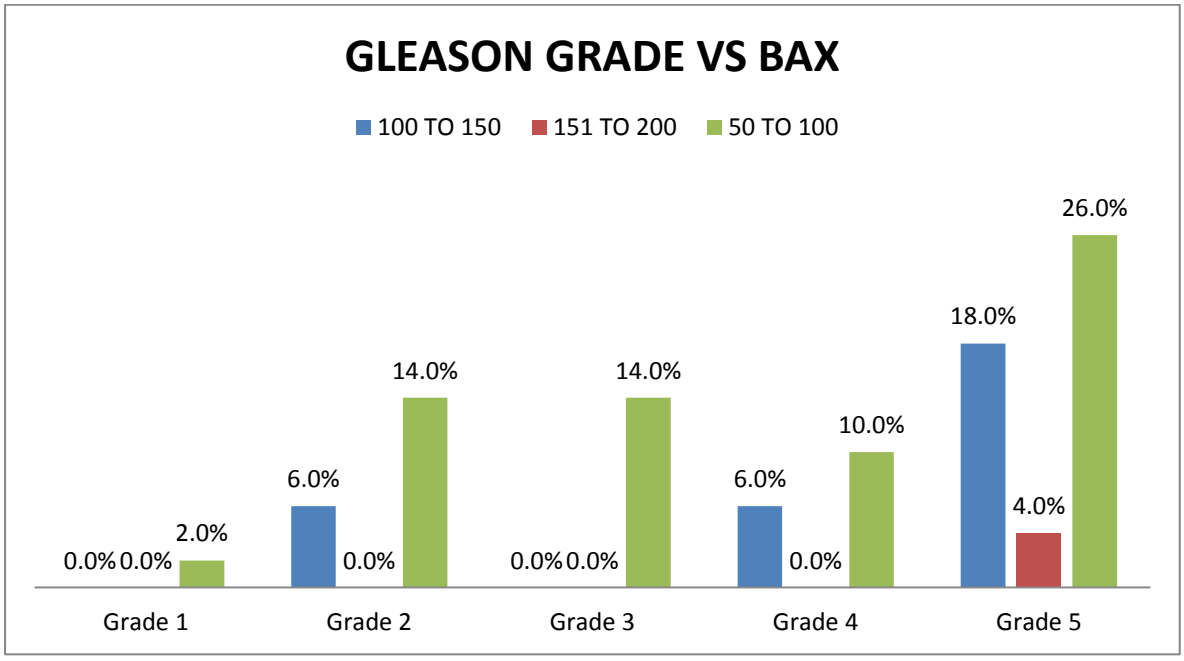



In present study Gleason grade 5 had n H-SCORE BCL2 score but the difference was no found to be significant difference found between these two categories.

**TABLE N0 22- H-SCORE BAX VS GLEASON GRADE**

| GLEASON GRADE | H SCORE BAX | | | | | |
|---|---|---|---|---|---|---|
| | 100 TO 150 | | 151 TO 200 | | 50 TO 100 | |
| | Count | N % | Count | N % | Count | N % |
| Grade 1 | 0 | 0.0% | 0 | 0.0% | 1 | 2.0% |
| Grade 2 | 3 | 6.0% | 0 | 0.0% | 7 | 14.0% |
| Grade 3 | 0 | 0.0% | 0 | 0.0% | 7 | 14.0% |
| Grade 4 | 3 | 6.0% | 0 | 0.0% | 5 | 10.0% |
| Grade 5 | **9** | **18.0%** | **2** | **4.0%** | **13** | **26.0%** |
| Total | 15 | 30.0% | 2 | 4.0% | 33 | 66.0% |
| P VALUE 0.5 | | | | | | |

**CHART N0 16 H-SCORE BAX VS GLEASON GRADE**

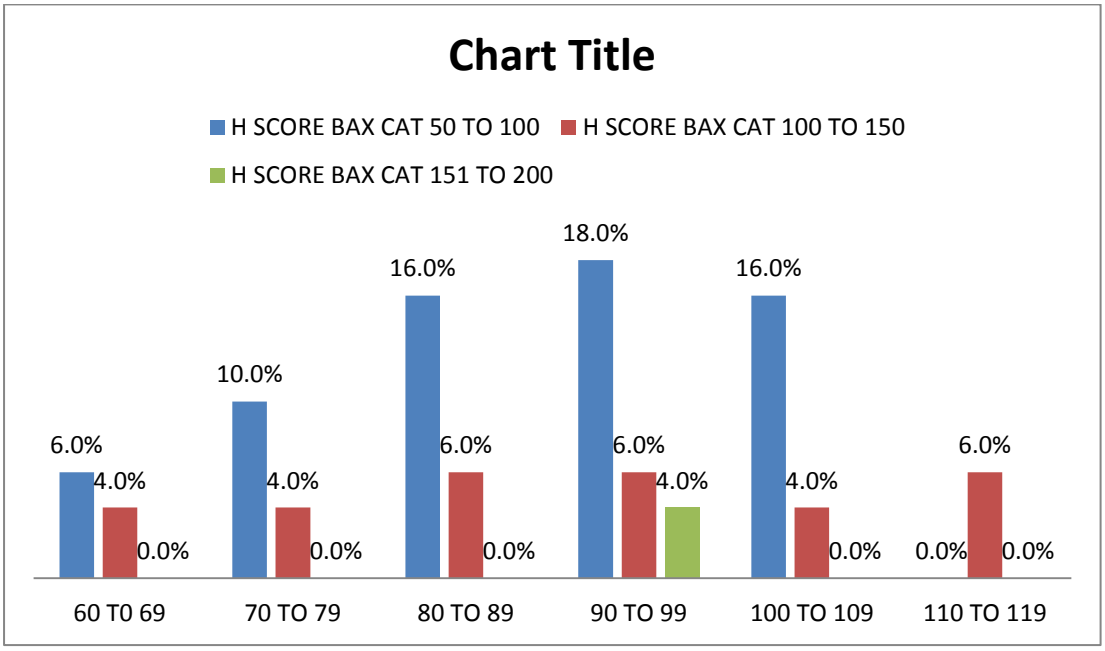



In present study Gleason grade 5 had high H-SCORE BAX score but the difference was no found to be significant difference found between these two categories.

## TABLE NO. 23- PSA VS H SCORE BAX

| PSA CATEGORIES | H SCORE BAX | | | | | |
|---|---|---|---|---|---|---|
| | 50 TO 100 | | 100 TO 150 | | 151 TO 200 | |
| | Count | N % | Count | N % | Count | N % |
| 60 T0 69 | 3 | 6.00% | 2 | 4.00% | 0 | 0.00% |
| 70 TO 79 | 5 | 10.00% | 2 | 4.00% | 0 | 0.00% |
| 80 TO 89 | 8 | 16.00% | 3 | 6.00% | 0 | 0.00% |
| 90 TO 99 | 9 | 18.00% | 3 | 6.00% | 2 | 4.00% |
| 100 TO 109 | 8 | 16.00% | 2 | 4.00% | 0 | 0.00% |
| 110 TO 119 | 0 | 0.00% | 3 | 6.00% | 0 | 0.00% |
| Total | 33 | 66.00% | 15 | 30.00% | 2 | 4.00% |
| P VALUE 0.2 | | | | | | |

## CHART NO. 17 PSA VS H SCORE BAX

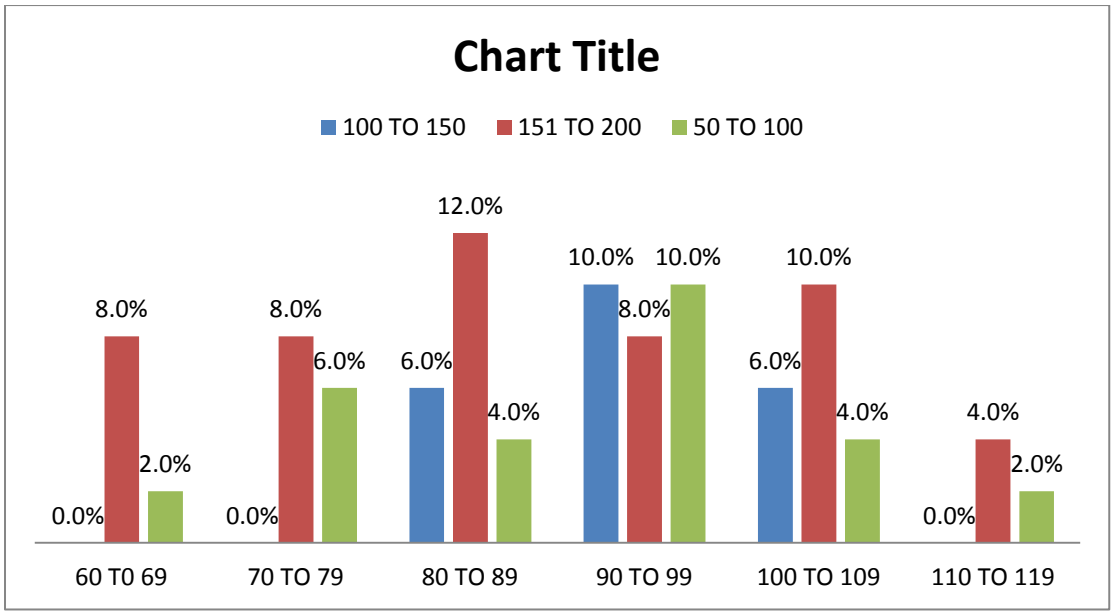



In present study PSA score grades had no association with H-SCORE BAX score.

## TABLE NO. 24 PSA VS H SCORE BCL2

| PSA CATEGORIES | H-SCORE BCL2 | | | | | |
|---|---|---|---|---|---|---|
| | 100 TO 150 | | 151 TO 200 | | 201 TO 250 | |
| | Count | N % | Count | N % | Count | N % |
| 60 T0 69 | 0 | 0.0% | 4 | 8.0% | 1 | 2.0% |
| 70 TO 79 | 0 | 0.0% | 4 | 8.0% | 3 | 6.0% |
| 80 TO 89 | 3 | 6.0% | 6 | 12.0% | 2 | 4.0% |
| 90 TO 99 | 5 | 10.0% | 4 | 8.0% | 5 | 10.0% |
| 100 TO 109 | 3 | 6.0% | 5 | 10.0% | 2 | 4.0% |
| 110 TO 119 | 0 | 0.0% | 2 | 4.0% | 1 | 2.0% |
| Total | 11 | 22.0% | 25 | 50.0% | 14 | 28.0% |
| P VALUE 0.5 | | | | | | |

## FIGURE NO. 18 PSA VS H SCORE BCL2

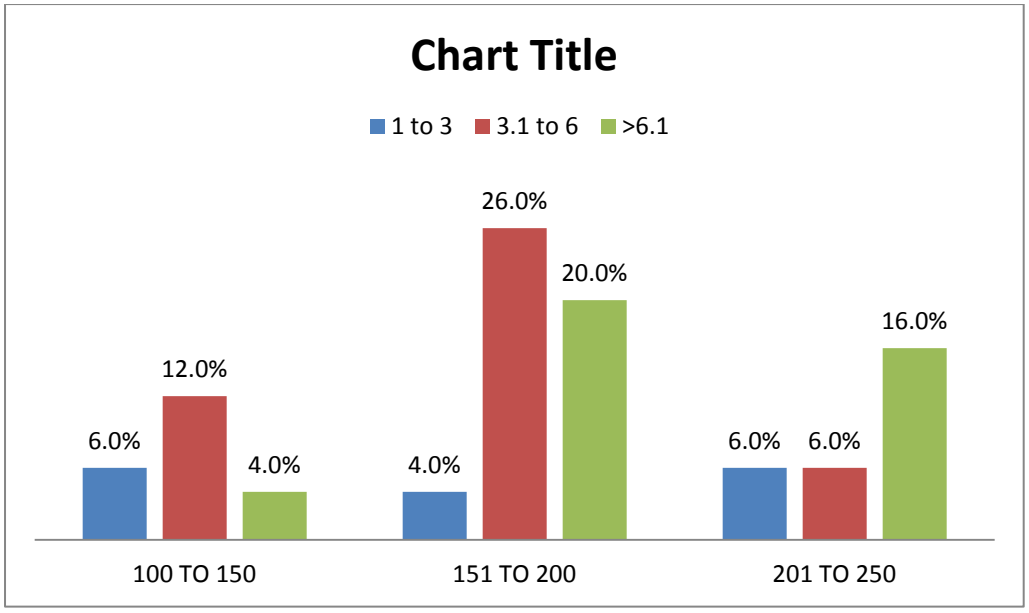



In present study PSA score grades had no association with H-SCORE BCL2 score.

## TABLE NO. 25-TUMOR SIZE VS H SCORE BCL2

| MRI/CT TUMOR SIZE cat | H-SCORE BCL2 | | | | | |
|---|---|---|---|---|---|---|
| | 100 TO 150 | | 151 TO 200 | | 201 TO 250 | |
| | Count | N % | Count | N % | Count | N % |
| 1 to 3 | 3 | 6.0% | 2 | 4.0% | 3 | 6.0% |
| 3.1 to 6 | 6 | 12.0% | 13 | 26.0% | 3 | 6.0% |
| >6.1 | 2 | 4.0% | 10 | 20.0% | 8 | 16.0% |
| Total | 11 | 22.0% | 25 | 50.0% | 14 | 28.0% |
| P VALUE 0.1 | | | | | | |

## CHART NO. 19 TUMOR SIZE VS H SCORE BCL2

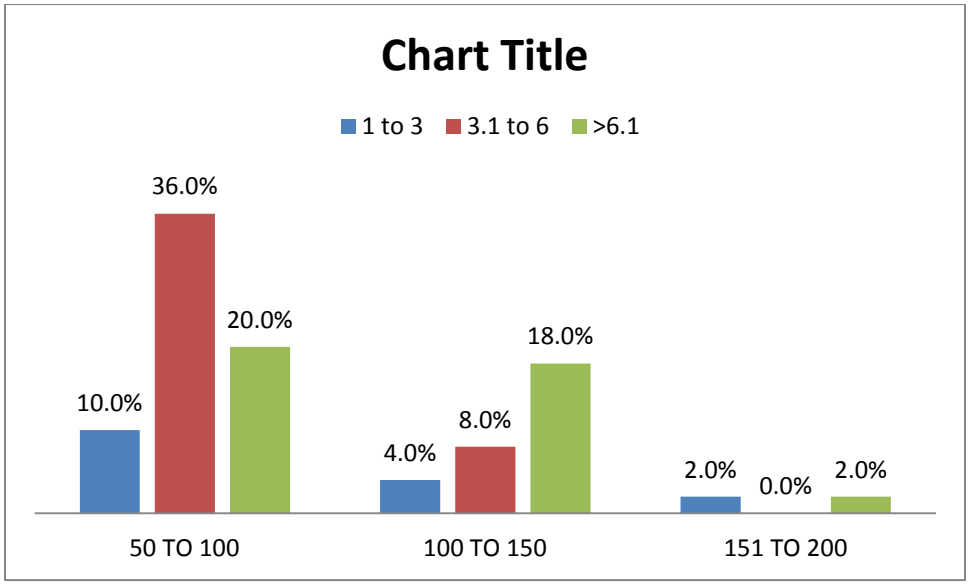



In present study Tumor size had no association with H-SCORE BCL2 score.

## TABLE NO. 26 TUMOR SIZE VS H SCORE BAX

| TUMOR SIZE | H SCORE BAX | | | | | |
|---|---|---|---|---|---|---|
| | 50 TO 100 | | 100 TO 150 | | 151 TO 200 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| 1 to 3 | 5 | 10.0% | 2 | 4.0% | 1 | 2.0% |
| 3.1 to 6 | 18 | 36.0% | 4 | 8.0% | 0 | 0.0% |
| >6.1 | 10 | 20.0% | 9 | 18.0% | 1 | 2.0% |
| Total | 33 | 66.0% | 15 | 30.0% | 2 | 4.0% |
| P VALUE 0.1 | | | | | | |

## CHART NO. 20 TUMOR SIZE VS H SCORE BAX

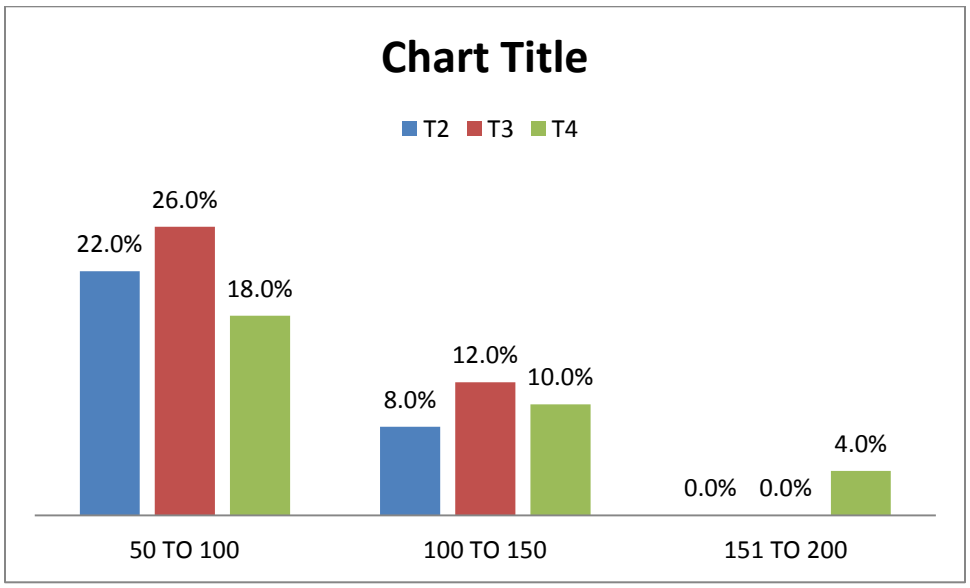



In present study Tumor size had no association with H-SCORE BAX score.

## TABLE NO. 27 STAGING VS H SCORE BAX

| CLINICAL STAGING | H SCORE BAX | | | | | |
|---|---|---|---|---|---|---|
| | 50 TO 100 | | 100 TO 150 | | 151 TO 200 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| T2 | 11 | 22.0% | 4 | 8.0% | 0 | 0.0% |
| T3 | 13 | 26.0% | 6 | 12.0% | 0 | 0.0% |
| T4 | 9 | 18.0% | 5 | 10.0% | 2 | 4.0% |
| Total | 33 | 66.0% | 15 | 30.0% | 2 | 4.0% |
| P VALUE 0.3 | | | | | | |

## CHART NO. 21 STAGING VS H SCORE BAX

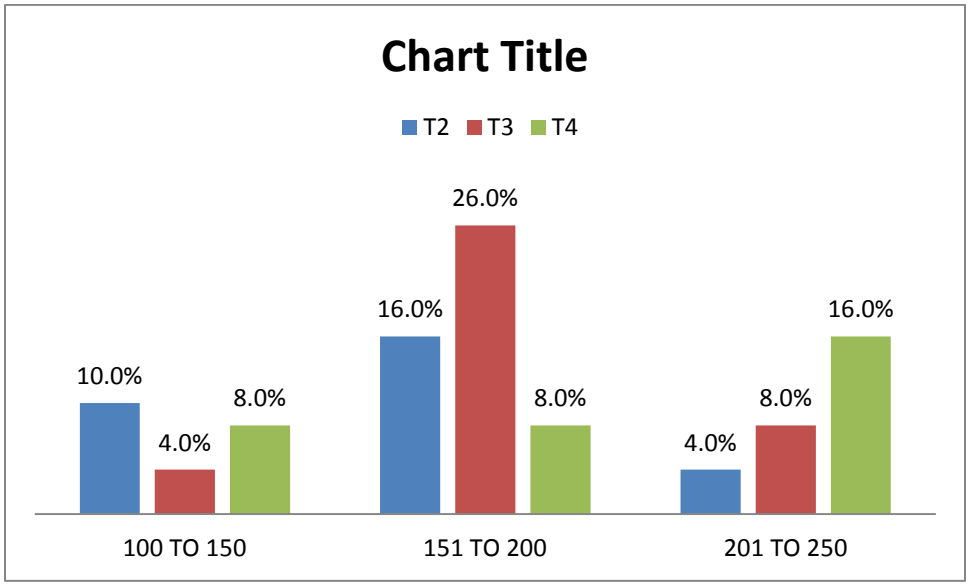



In present study Clinical Staging had no association with H-SCORE BAX score.

**TABLE NO. 28 STAGING VS H SCORE BCL2**

| CLINICAL STAGING | H-SCORE BCL2 | | | | | |
|---|---|---|---|---|---|---|
| | 100 TO 150 | | 151 TO 200 | | 201 TO 250 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| T2 | 5 | 10.0% | 8 | 16.0% | 2 | 4.0% |
| T3 | 2 | 4.0% | 13 | 26.0% | 4 | 8.0% |
| T4 | **4** | **8.0%** | **4** | **8.0%** | **8** | 16.0% |
| Total | 11 | 22.0% | 25 | 50.0% | 14 | 28.0% |
| P VALUE | | | | | | |

**CHART NO. 22 STAGING VS H SCORE BCL2**

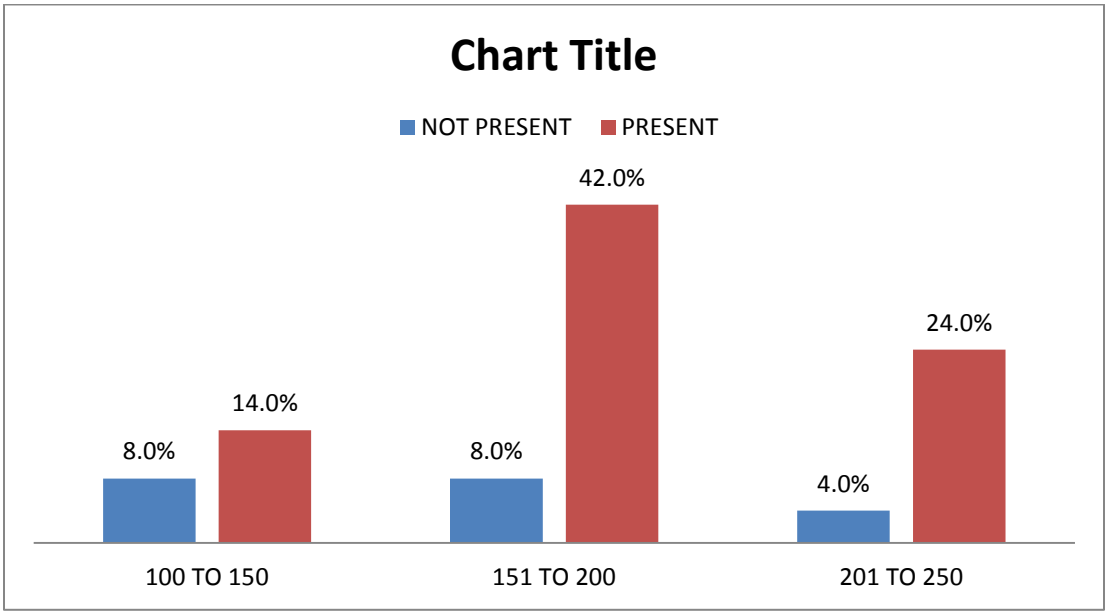



In present study Clinical Staging had high H-SCORE BCL2 score but the difference was not found to be significant.

## TABLE NO. 29 METASTASIS VS H SCORE BCL2

| METASTASIS | H-SCORE BCL2 | | | | | |
|---|---|---|---|---|---|---|
| | 100 TO 150 | | 151 TO 200 | | 201 TO 250 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| NOT PRESENT | 4 | 8.0% | 4 | 8.0% | 2 | 4.0% |
| PRESENT | 7 | 14.0% | 21 | 42.0% | 12 | 24.0% |
| Total | 11 | 22.0% | 25 | 50.0% | 14 | 28.0% |
| P VALUE 0.3 | | | | | | |

## CHART NO. 23 METASTASIS VS H SCORE BCL2

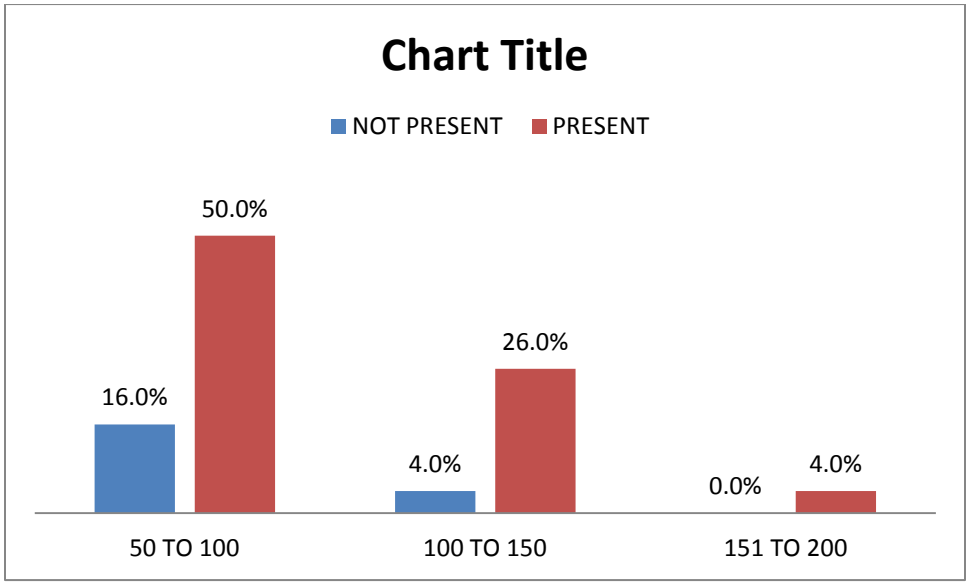



In present study presence of metastasis had no association with H-SCORE BCL2 score.

## TABLE NO. 30 METASTASIS VS H SCORE BAX

| METASTASIS | H SCORE BAX | | | | | |
|---|---|---|---|---|---|---|
| | 50 TO 100 | | 100 TO 150 | | 151 TO 200 | |
| | Count | Table N % | Count | Table N % | Count | Table N % |
| NOT PRESENT | 8 | 16.0% | 2 | 4.0% | 0 | 0.0% |
| PRESENT | 25 | 50.0% | 13 | 26.0% | 2 | 4.0% |
| Total | 33 | 66.0% | 15 | 30.0% | 2 | 4.0% |
| 0.5 | | | | | | |

## CHART NO. 24 METASTASIS VS H SCORE BAX

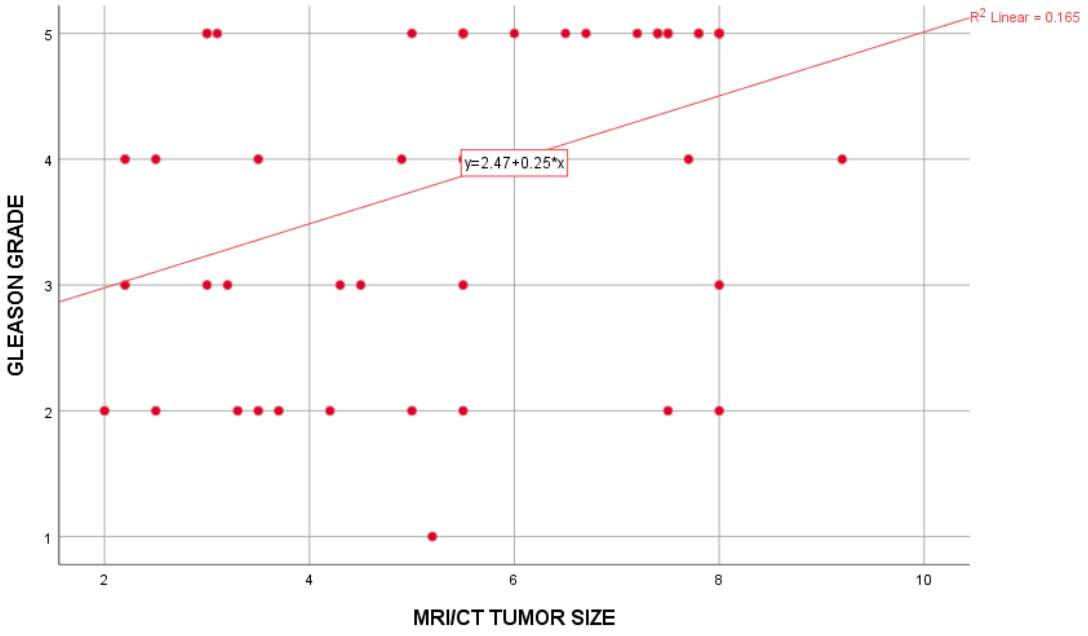



In present study presence of metastasis had no association with H-SCORE BAX score.

## TABLE NO. 31 GLEASON GRADE VS MRI/CT TUMOR SIZE

| Correlations | | | |
|---|---|---|---|
| | | GLEASON GRADE | MRI/CT TUMOR SIZE |
| GLEASON GRADE | Pearson Correlation | 1 | .406** |
| | Sig. (2-tailed) | | 0.003 |
| | N | 50 | 50 |
| MRI/CT TUMOR SIZE | Pearson Correlation | .406** | 1 |
| | Sig. (2-tailed) | 0.003 | |
| | N | 50 | 50 |
| **. Correlation is significant at the 0.01 level (2-tailed). | | | |

## CHART NO. 25 GLEASON GRADE VS MRI/CT TUMOR SIZE

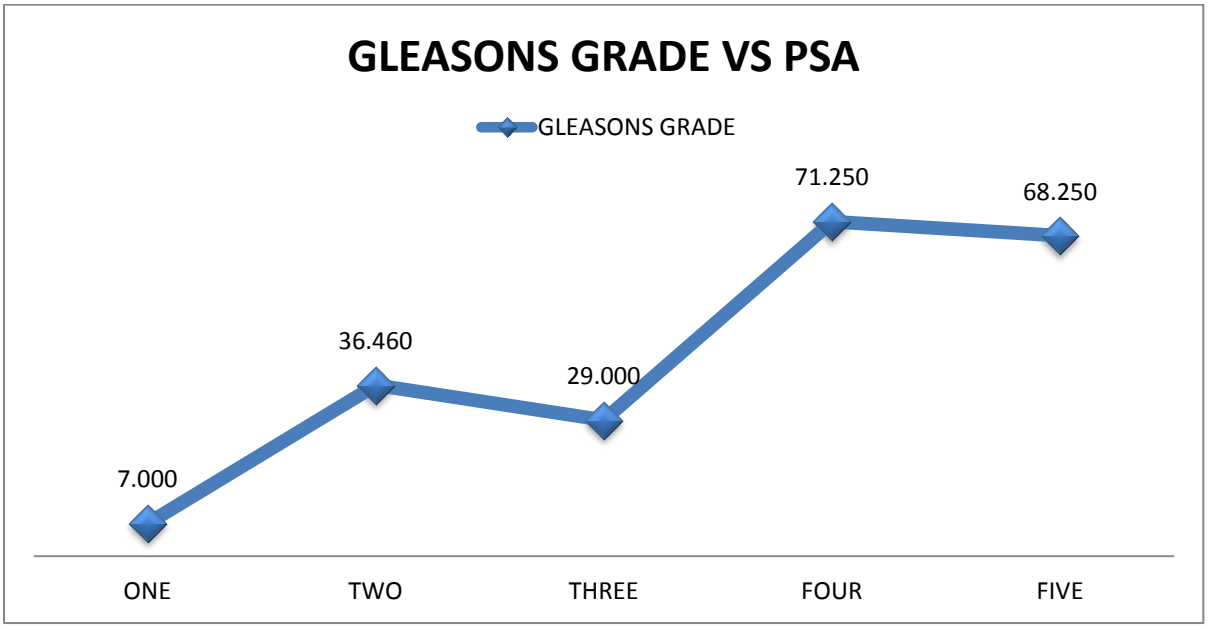



There was a moderate positive correlation was found between Gleason Grade and tumor size

## TABLE NO. 32-GLEASON GRADE VS PSA LEVELS

| ANOVA TEST | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| PSA levels | | | | | | | | |
| GLEASONS GRADE | N | Mean | Std. Deviation | Std. Error | 95% Confidence Interval for Mean | | F VALUE | P VALUE |
| | | | | | Lower Bound | Upper Bound | | |
| ONE | 1 | 7.000 | | | | | 6 | 0.001 |
| TWO | 10 | 36.460 | 41.6897 | 13.1834 | 6.637 | 66.283 | | |
| THREE | 7 | 29.000 | 12.8841 | 4.8697 | 17.084 | 40.916 | | |
| FOUR | 8 | 71.250 | 28.6942 | 10.1449 | 47.261 | 95.239 | | |
| FIVE | 24 | 68.250 | 19.3351 | 3.9468 | 60.085 | 76.415 | | |
| Total | 50 | 55.652 | 31.2261 | 4.4160 | 46.778 | 64.526 | | |

## CHART NO. 26 GLEASON GRADE VS PSA LEVELS

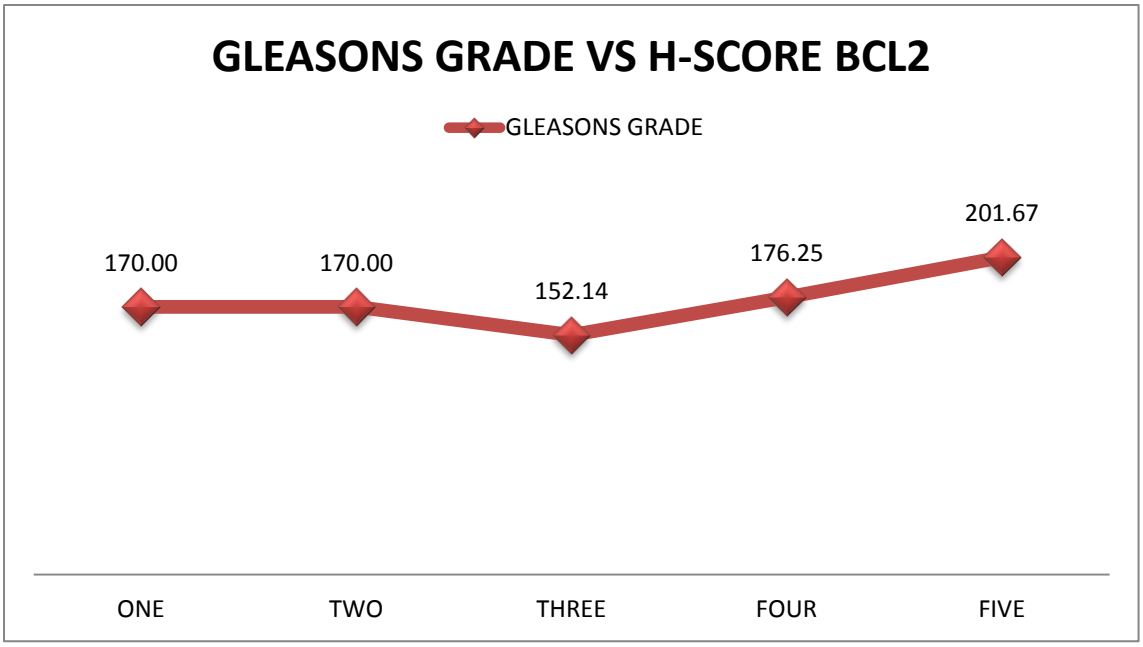



In present study, men values of PSA were increasing manner with Gleason's grade except at 3rd grade, and it was found to be significant.

## TABLE NO. 33- GLEASON GRADE VS H-SCORE BCL2

| ANOVA TEST | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| H-SCORE BCL2 | | | | | | | | |
| GLEASONS GRADE | N | Mean | Std. Deviation | Std. Error | 95% Confidence Interval for Mean | | F VALUE | P VALUE |
| | | | | | Lower Bound | Upper Bound | | |
| ONE | 1 | 170.00 | | | | | 4 | 0.009 |
| TWO | 10 | 170.00 | 36.818 | 11.643 | 143.66 | 196.34 | | |
| THREE | 7 | 152.14 | 31.867 | 12.044 | 122.67 | 181.61 | | |
| FOUR | 8 | 176.25 | 39.619 | 14.007 | 143.13 | 209.37 | | |
| FIVE | 24 | 201.67 | 30.024 | 6.129 | 188.99 | 214.34 | | |
| Total | 50 | 183.70 | 37.044 | 5.239 | 173.17 | 194.23 | | |

## CHART NO. 27 GLEASON GRADE VS H-SCORE BCL2

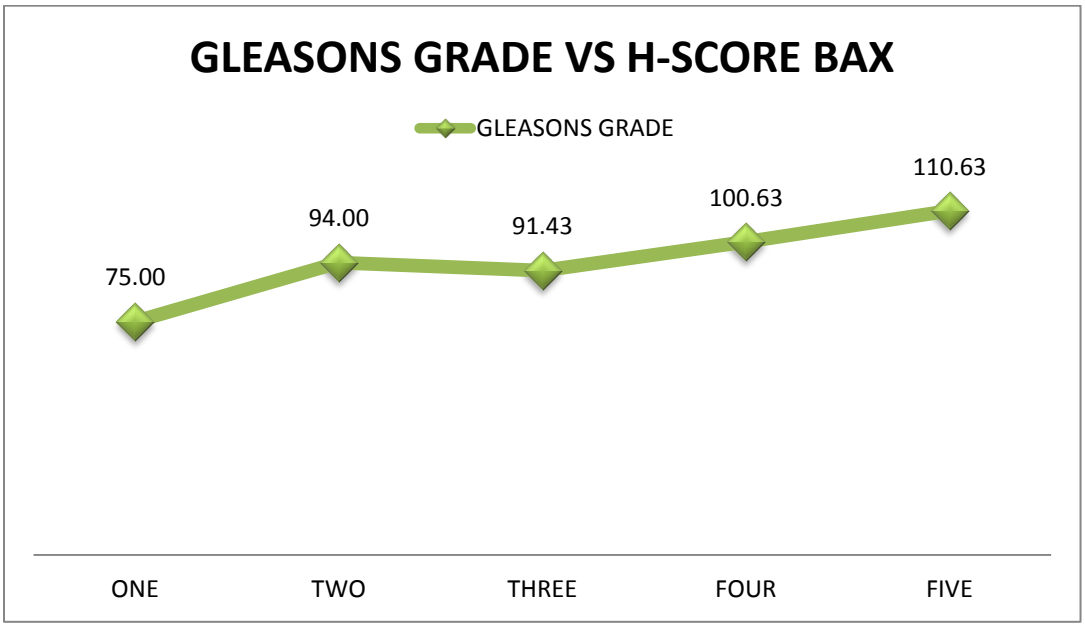



In present study, men values of PSA were increasing manner with H-SCORE BCL2 except at 3rd grade, and it was not found to be significant.

## TABLE NO. 34 GLEASON GRADE VS H-SCORE BAX

| ANOVA TEST | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| H SCORE BAX | | | | | | | | |
| GLEASON GRADE | N | Mean | Std. Deviation | Std. Error | 95% Confidence Interval for Mean | | F VALUE | P VALUE |
| | | | | | Lower Bound | Upper Bound | | |
| ONE | 1 | 75.00 | | | | | 2 | 0.160 |
| TWO | 10 | 94.00 | 22.211 | 7.024 | 78.11 | 109.89 | | |
| THREE | 7 | 91.43 | 6.268 | 2.369 | 85.63 | 97.23 | | |
| FOUR | 8 | 100.63 | 20.777 | 7.346 | 83.25 | 118.00 | | |
| FIVE | 24 | 110.63 | 28.258 | 5.768 | 98.69 | 122.56 | | |
| Total | 50 | 102.30 | 24.748 | 3.500 | 95.27 | 109.33 | | |

## CHART NO. 28 GLEASON GRADE VS H-SCORE BAX

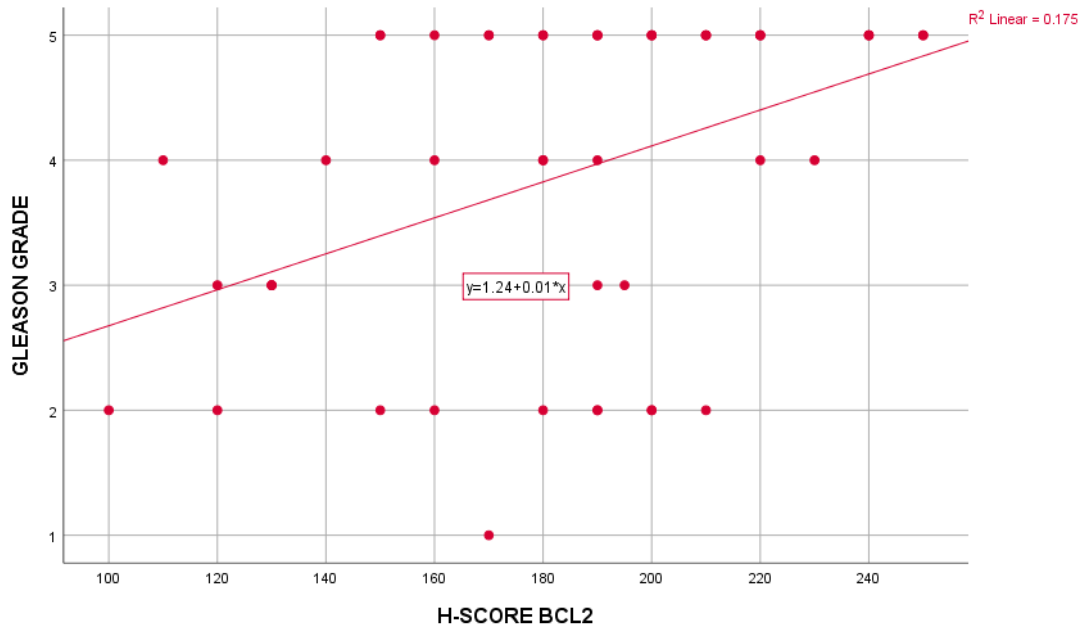



In present study, men values of H SCORE BAX were increasing manner with GLEASON GRADE except at 3rd grade, and it was not found to be significant.

## TABLE NO. 35 GLEASON GRADE VS H-SCORE BCL2

| Correlations | | | |
|---|---|---|---|
| | | GLEASON GRADE | H-SCORE BCL2 |
| GLEASON GRADE | Pearson Correlation | 1 | .419** |
| | Sig. (2-tailed) | | 0.002 |
| | N | 50 | 50 |
| H-SCORE BCL2 | Pearson Correlation | .419** | 1 |
| | Sig. (2-tailed) | 0.002 | |
| | N | 50 | 50 |
| **. Correlation is significant at the 0.01 level (2-tailed). | | | |

## CHART NO. 29 GLEASON GRADE VS H-SCORE BCL2

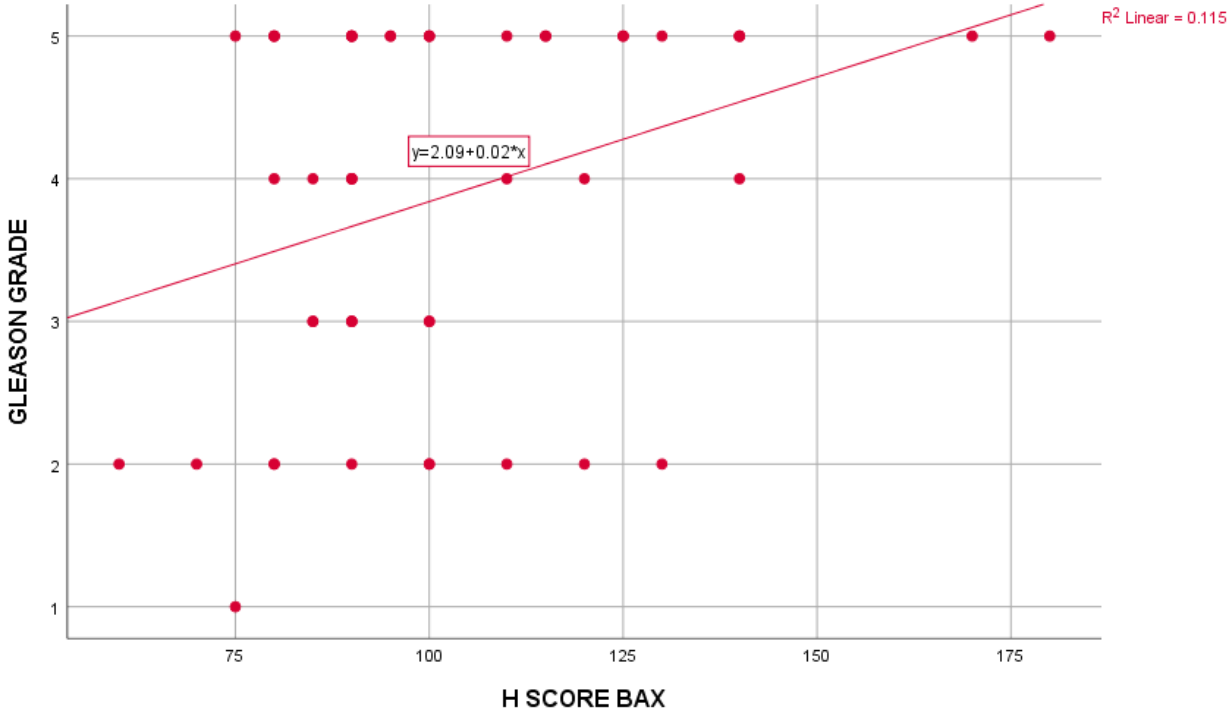



There was a moderate positive correlation was found between Gleason Grade and H-SCORE BCL2 and it was found to be significant.

## TABLE NO. 36 GLEASON GRADE VS H-SCORE BAX

| Correlations | | | |
|---|---|---|---|
| | | GLEASON GRADE | H SCORE BAX |
| GLEASON GRADE | Pearson Correlation | 1 | .340* |
| | Sig. (2-tailed) | | 0.016 |
| | N | 50 | 50 |
| H SCORE BAX | Pearson Correlation | .340* | 1 |
| | Sig. (2-tailed) | 0.016 | |
| | N | 50 | 50 |
| *. Correlation is significant at the 0.05 level (2-tailed). | | | |

## CHART NO. 30 GLEASON GRADE VS H-SCORE BAX

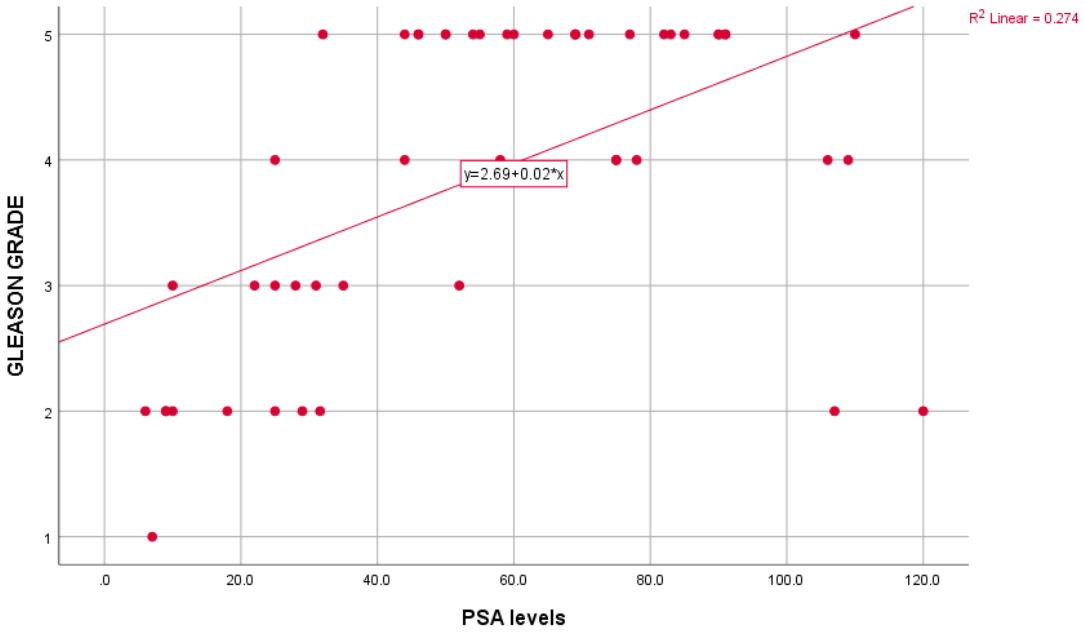



There was a mild positive correlation was found between Gleason Grade and H-SCORE BAX and it was found to be significant.

## TABLE NO. 37 GLEASON GRADE VS PSA LEVEL

| Correlations | | | |
|---|---|---|---|
| | | GLEASON GRADE | PSA levels |
| GLEASON GRADE | Pearson Correlation | 1 | .523** |
| | Sig. (2-tailed) | | 0.000 |
| | N | 50 | 50 |
| PSA levels | Pearson Correlation | .523** | 1 |
| | Sig. (2-tailed) | 0.000 | |
| | N | 50 | 50 |
| **. Correlation is significant at the 0.01 level (2-tailed). | | | |

## CHART NO. 31 GLEASON GRADE VS PSA LEVEL

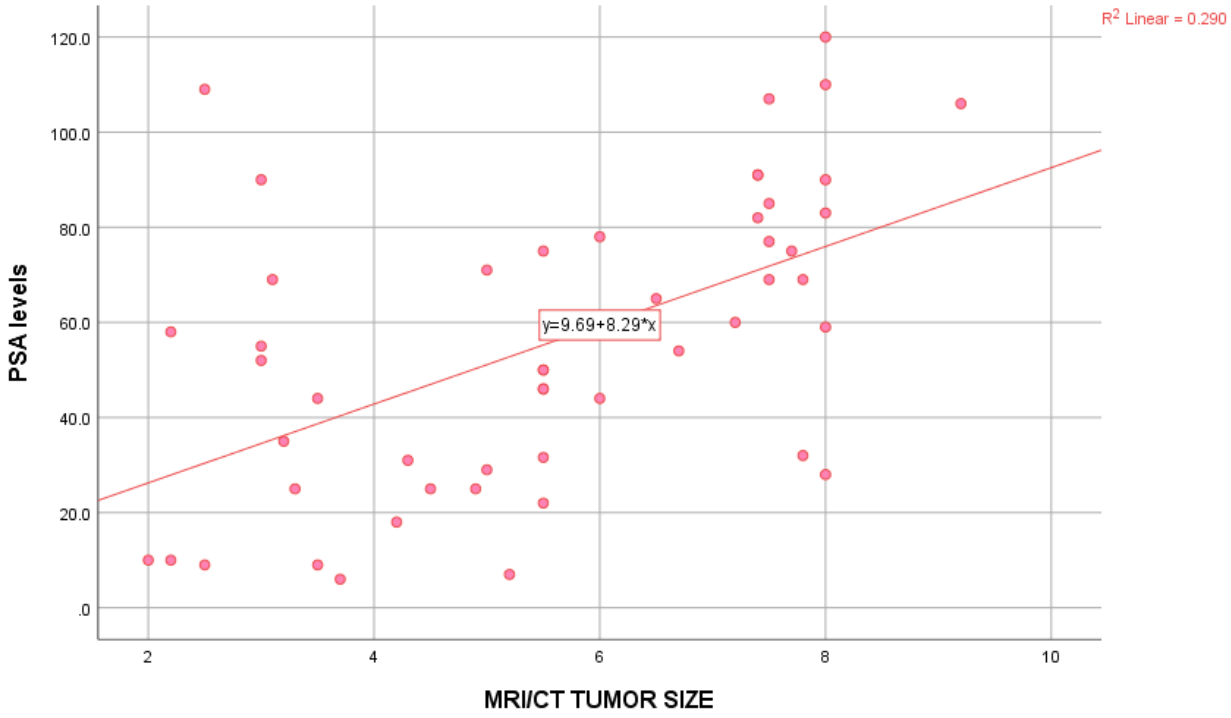



There was a moderate positive correlation was found between Gleason Grade and PSA levels and it was found to be significant.

## TABLE NO. 38 MRI/CT TUMOR SIZE VS PSA LEVELS

| Correlations | | | |
|---|---|---|---|
| | | MRI/CT TUMOR SIZE | PSA levels |
| MRI/CT TUMOR SIZE | Pearson Correlation | 1 | .539** |
| | Sig. (2-tailed) | | 0.000 |
| | N | 50 | 50 |
| PSA levels | Pearson Correlation | .539** | 1 |
| | Sig. (2-tailed) | 0.000 | |
| | N | 50 | 50 |
| **. Correlation is significant at the 0.01 level (2-tailed). | | | |

## CHART NO. 32 MRI/CT TUMOR SIZE VS PSA LEVELS

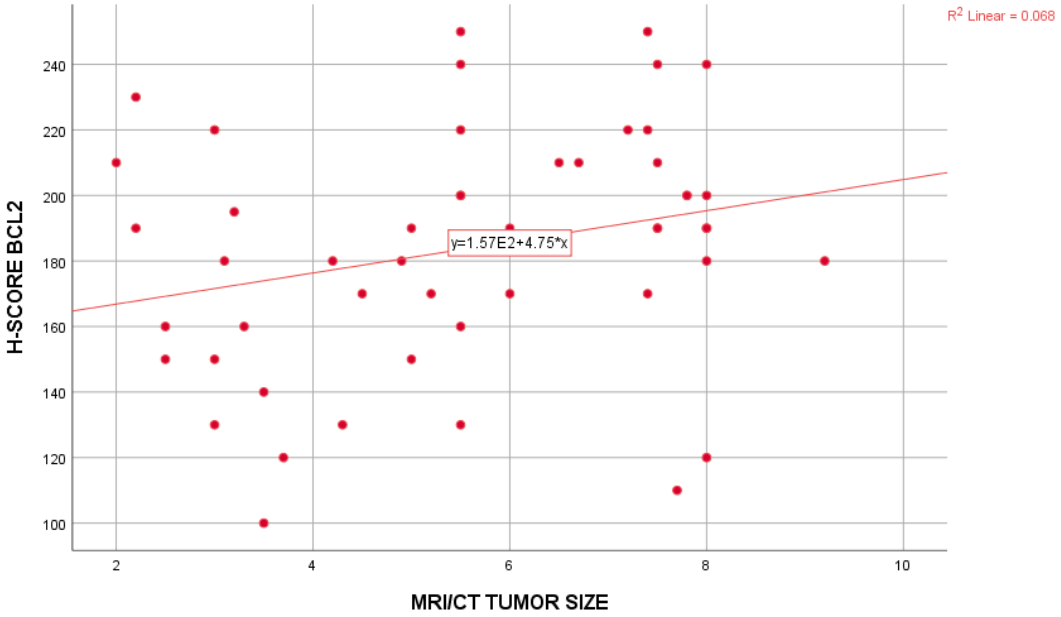



There was a moderate positive correlation was found between PSA levels and tumor size and it was found to be significant.

## TABLE NO. 39 MRI/CT TUMOR SIZE VS H-SCORE BCL2

| Correlations | | | |
|---|---|---|---|
| | | MRI/CT TUMOR SIZE | H-SCORE BCL2 |
| MRI/CT TUMOR SIZE | Pearson Correlation | 1 | 0.261 |
| | Sig. (2-tailed) | | 0.068 |
| | N | 50 | 50 |
| H-SCORE BCL2 | Pearson Correlation | 0.261 | 1 |
| | Sig. (2-tailed) | 0.068 | |
| | N | 50 | 50 |

## CHART NO. 33 MRI/CT TUMOR SIZE VS H-SCORE BCL2

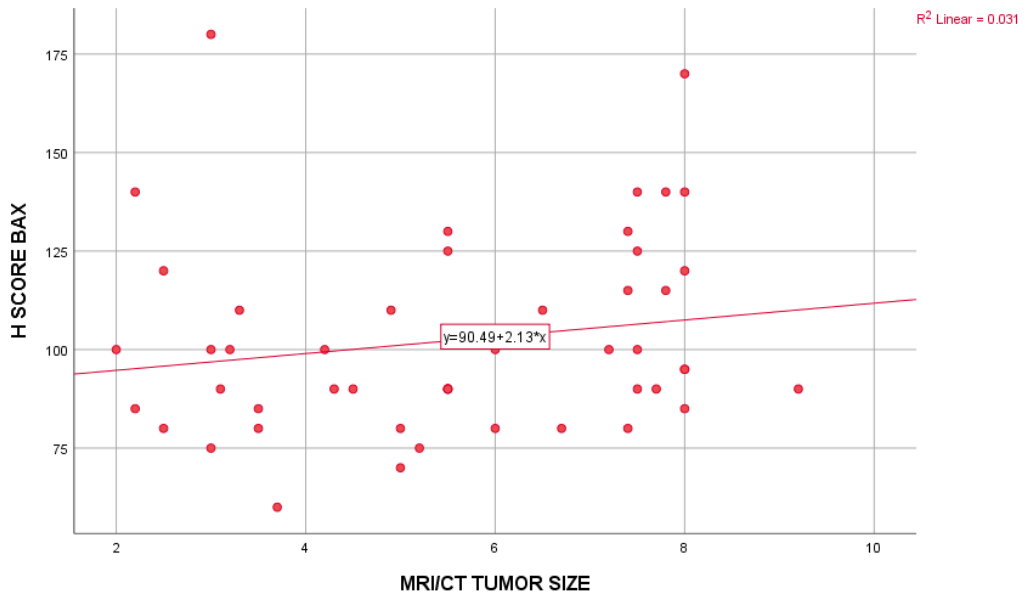



There was a mild positive correlation was found between tumor size and H-SCORE BCL2 and there was no significance found.

## TABLE NO. 40 MRI/CT TUMOR SIZE VS H SCORE BAX

| Correlations | | | |
|---|---|---|---|
| | | MRI/CT TUMOR SIZE | H SCORE BAX |
| MRI/CT TUMOR SIZE | Pearson Correlation | 1 | 0.175 |
| | Sig. (2-tailed) | | 0.225 |
| | N | 50 | 50 |
| H SCORE BAX | Pearson Correlation | 0.175 | 1 |
| | Sig. (2-tailed) | 0.225 | |
| | N | 50 | 50 |

## CHART NO. 34 MRI/CT TUMOR SIZE VS H SCORE BAX




There was no positive correlation was found between Tumor size and H SCORE BAX.

# DISCUSSION

# DISCUSSION

Prostate cancer has a variety of clinical behaviors, from slow-growing tumors to aggressive, fatal malignancies. Clinical stage, grade, and blood levels of prostate-specific antigen (PSA) are clinical prognostic factors that are the predictors of recurrence after therapy .

According to several studies, emergence of cancer has been associated with altered role of apoptosis and the expression of certain apoptotic genes is associated with tumors with high Gleason scores.[43-46] Most research on these relationships has been done outside India, and little information is available. Therefore, the present study is to determine if BAX and BCL2 expression genes correlated with Gleason scores in prostate cancer.

The median age of presentation is 68 years old, and it is typically thought of as an older person's cancer. However, 10% of new diagnoses in the USA involve males under the age of 55.[47] As people age, their risk of acquiring prostate cancer increases.. In the present study, the predominant study population is in the 61 -70 years (46%), 71 - 80 years (34%)

This may reflect the diagnosis of early-onset prostate cancer, a condition that is increasingly recognized yet unappreciated, as well as the more widespread screening practices that are currently in use.[47]

Based on the existing literature, men under the age of 40 have had 30 recorded instances of prostate cancer, with an incidence of 0.8-1.1%.[48-50]

Burning micturition, Urinary hesitation & dribbling were common symptoms followed by Urinary retention in the present study.

Although irritable voiding symptoms (frequency, urgency, and dysuria) can be the early manifestation, bladder cancer patients typically arrive with painless hematuria (grossly apparent or microscopic).

In present study majority of the study population had metastasis (80%). T indicates The diagnosis is typically not made until the tumour is locally progressed or metastatic, despite the availability of good tests for early identification and effective treatments for tumours so found. However, doctors are hesitant to employ these tests out of concern that many malignancies would be latent, posing little harm to the host's life or health, and that treatment would result in unwarranted morbidity.

According to a recent study from Keck Medicine of USC[51], men 45 and older are now more likely to have metastatic prostate cancer than they were five years ago. This finding is in line with recommendations against annual prostate cancer screenings.

In present study majority of the study population had H-SCORE BAX of 50 TO 100 (66%) followed by 100 TO 150 (30%). In present study majority of the study population had H-SCORE BCL2 of 151 TO 200 (50%) followed by 201 TO 250 (28%).

**GLEASON'S GRADE VS PSA**

In present study, men values of PSA were increasing manner with Gleason's grade except at 3rd grade, and it was found to be significant on ANOVA test. There was a remarkable relationship between Gleason Grade and PSA levels and it was found to be significant (r=0.54).

This indicates till grade 2 PSA levels may increase, will be stagnant at grade 3 (29 – 37 PSA level) and four and fifth grade had increased levels of PSA ranging from 68 to 72. Overall there is an moderate increase PSA levels along with the increasing Gleason's grade, means higher levels predicts the severity and prognosis of prostate cancer.

**H-SCORE BCL2 vs PSA**

In present study, men values of PSA were increasing manner with H-SCORE BCL2 except at 3rd grade, and it was not found to be significant which is supported by **Anvari K, et al.[39] which** showed high correlation between Gleason Grade and H-SCORE BCL2.

**GLEASON GRADE VS TUMOR SIZE**

There was a remarkable relationship between Gleason Grade and tumor size (r=0.4).

Correlation of the Gleason score with tumor volume (r = 0.4) **Friedersdorff F et al.[52]**The Gleason score does not correspond as significantly with the tumor volume as the Prostate Health Index (PHI) does in their study which is not explored in our study.

**GLEASON GRADE VS H-SCORE BCL2**

There was remarkable relationship between Gleason Grade and H-SCORE BCL2 and it was found to be significant(r=0.42). A strong association with the cell survival markers Ki-67 and bcl-2 suggests that it contributes to the development of tumour cells according to **Amirghofran Z et al.[44]** which supports present study.

22/40 (55%) of the 40 adenocarcinoma cases under study of **Alshahmi E. et al[53].** had Bcl-2 protein immunostaining that was positive.

. According to their research, bcl-2 immunostaining is more common in tumour samples and is linked to higher advanced Gleason scores, demonstrating that a rise in the ratio of this anti-apoptotic protein occurs frequently during prostate cancer growth which is supporting present study.

On the other hand, There was no remarkable relationship between aberrant bcl-2 expression and grading in **Khor L-Y et al[54].** study which doesn't support present study.

16 of 64 (25%) adenocarcinomas expressed the anti-apoptotic protein Bcl-2, which tended to be more prevalent in high-grade tumours (Gleason grade 8 to 10; 41%) and nodal metastases (38%) than in lower-grade (Gleason 2 to 7) in **Krajewska M et al[55].**study which supports our study.

**Anvari K, et al.[39]** showed high correlation between Gleason Grade and H-SCORE BCL2.

**GLEASON GRADE VS H-SCORE BAX**

In present study, men values of H SCORE BAX were increasing manner with GLEASON GRADE except at 3rd grade, and it was not found to be significant in ANOVA test. There was a mild remarkable relationship between Gleason Grade and H-SCORE BAX and it was found to be significant (r=0.34) in pearsons correlation.

An aberrant bax expression and higher Gleason score were shown to have a marginally significant connection (p 0.08) in a study done by **Khor L-Y et al.[54]** which supports present study.

**Anvari K, et al.**[39]showed no correlation between Gleason Grade and H-SCORE BAX.

Bax expression was highest in foci with perineural invasion and was substantially higher in Gleason grade 3 ans 5 cancer than Gleason grade 2 carcinoma in a finland based study by **Tolonen TT, et al**[43] .

**GLEASON GRADE VS PSA**

There was remarkable relationship between Gleason Grade and PSA levels and it was found to be significant (r=0.54).

A japan based study (**Yoshino T et al**[56]**.**) showed indirect predictor of Carcinoma prostate.

**TUMOR SIZE VS PSA**

There was remarkable relationship between PSA levels and tumor size and it was found to be significant (r=0.54).

**Aihara M et al.**[57] which is almost similar to present study.

**TUMOR SIZE AND H-SCORE BCL2 & BAX**

There was mild remarkable relationship between tumor size and H-SCORE BCL2 and there was no significance found. The limitation of this study is it is uni centric and sample size is relatively small to come to a significant conclusion.

# CONCLUSION

# CONCLUSION

This study concluded that PSA levels in cases of prostate cancer patients were showing increasing trend with Gleasons grade and found to be significant on ANOVA test. It also showed there was high correlation between Gleason grade and H score BCL2, but not that significant with Bax gene. As there is moderate increase PSA levels with increasing Gleason grade, which reveals higher levels predict the severity and prognosis of prostate cancer. BCL2 expression which is more common in tumor tissues & linked to higher advanced Gleason grade, which demonstrates rise in anti apoptotic protein occurs more often in prostate cancers. To the best of our knowledge review of literature did not show any Indian study to show the correlation of bax and bcl2 gene with Gleason grade in prostate cancer cases. This study is a maiden attempt to understand the pathogenesis of Bax and bcl2 in the development of prostate carcinoma and its significance with increasing grade of the tumor , PSA levels with increasing grade of the tumor hence it will be of utmost usage for clinicans in future for targeted immunotherapy in long term prognosis of the patients.

# SUMMARY

# SUMMARY

1. The present study was conducted in the Department of Pathology , Sri Devaraj Urs Medical College, Tamaka, Kolar from December 2020 to October 2022. Also retrospective cases from January 2015 to November 2019 were included in the study.
2. A total of 50 cases were studied and majority of the patients were in-between age of 61-70 years.
3. In the present study , majority of the cases was in gleason grade 5(42%), PSA levels was in range 90-99(28%), tumor size in range of 3.1-6 cm(44%), T4 stage (34%) ,metastasis (80%).
4. There was positive correlation between gleason grade and tumor size & levels of PSA were in increasing manner with gleason s grade except at $3^{rd}$ grade and was significant.
5. There was positive correlation between gleason grade and H-score bcl2 , suggesting the contribution of bcl2 to development of tumor cells , but not significant with bax gene
6. Furthur studies on the association of these antiapoptotic and pro apoptotic proteins with prostate cancer cases can pave the way for the advanced treatment for the patients in future.

# LIMITATION

## LIMITATIONS OF THIS STUDY

1. 1.The sample size of this study is relatively small(n=50) to derive at a significant conclusion.
2. 2..The study was done in a unicentric basis, hence results might vary if we do the study in multicentric range.
3. 3.. Follow up for most of the cases was of limited data as the patients didn't turn up for the further treatment.

# BIBLIOGRAPHY

# BIBLIOGRAPHY


1. The Global Cancer Observatory, Globocan 2020. International Agency for Research on Cancer. Prostate cancer factsheet.https://gco.iarc.fr/today/data/factsheets/cancers/27-Prostate-fact-sheet.pdf
2. Gandaglia G, Leni R, Bray F, Fleshner N, Freedland SJ, Kibel A, et al. Epidemiology and prevention of prostate cancer. Eur Urol Oncol . 2021;4(6):877–92.
3. Hariharan K, Padmanabha V. Demography and disease characteristics of prostate cancer in India. Indian J Urol 2016;32:103-8.
4. Dhillon PK, Mathur P, Nandakumar A, Fitzmaurice C, Kumar GA, Mehrotra R, et al. The burden of cancers and their variations across the states of India: The Global Burden of Disease Study 1990–2016. Lancet Oncol 2018;19:1289–306.
5. Qian J, Jenkins RB, Bostwick DG. Determination of gene and chromosome dosage in prostatic intraepithelial neoplasia and carcinoma. Anal Quant Cytol Histol. 1998;20:373-80.
6. Xu J, Zheng SL, Isaacs SD, et al. Inherited genetic variant predisposes to aggressive but not indolent prostate cancer. Proc Natl Acad Sci U S A. 2010;107:2136-40.
7. Kattan MW, Eastham JA, Stapleton AM, Wheeler TM, Scardino PT. A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer. J Natl Cancer Inst. 1998;90:766-71.
8. Hartwell LH, Kastan MB. Cell cycle controland cancer. Science. 1994;266:1821-8.
9. Lane DP. Cancer. p53, guardian of the genome. Nature. 1992;358:15-6.
10. Torrealba N, Roderiguez-Berriguete G, Fraile F et al. PI3K pathway and Bcl2 family. Clinicopathological Features in prostate cancer. The Aging Male 2018;21:211-213.

11. Jain S, Saxena S, Kumar A. Epidemiology of prostate cancer in India. Meta Gene. 2014;2:596–605.
12. Bindra Singh, S Das, R Kalyani, HML Kumar,Cancer profile in Kolar: A ten years study, Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs University, Kolar, India ,Indian Journal of Cancer. 2010;47:160-165.
13. Gleason DF. Histologic grading and clinical staging of prostate carcinoma. In: Tannenbaum M, editor. Urologic pathology: the prostate. Philadelphia: Lea & Fibiger, 1977:171-98
14. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68 :394- 424.
15. Shapiro E, Hartanto V, Lepor H. Quantifying the smooth muscle content of the prostate using double-immunoenzymatic staining and color assisted image analysis. J. Urol. 1992; 147:1167–1170.
16. Josso N. Physiology of Sex Differentiation. Pediat. Adolesc. Endocr. 1981; 8:1–13.
17. Marker PC, Donjacour AA, Dahiya R, Cunha GR. Hormonal, cellular, and molecular control of prostatic development. Dev Biol. Jan 15; 2003 253:165–174
18. Rosai J, Ackerman's. The Prostate and seminal vesical. In: Rosai, Ackerman, editors. Surgical Pathology, Vol 2 (11th edition). New Delhi: Mosby. 2018; 1097-98
19. Cancer Stat Facts: Prostate Cancer [Internet]. SEER, 2018. Available from: https://seer.cancer.gov/statfacts/html/prost.html.

20. SEER Cancer Statistics Review, 1975-2013 [Internet]. National Cancer Institue, Bethesda, MD. 2016. Available from: https://seer.cancer.gov/csr/1975_2015/. Accessed 04 February 2019.[Internet].SEER,2018.Available- https://seer.cancer.gov /explorer/application.php
21. Ferris-i-Tortajada J, Garcia-i-Castell J, Berbel-Tornero O, Ortega-Garcia JA. [Constitutional risk factors in prostatecancer]. Actas Urol Esp. 2011;35 :282-288
22. Sridhar G, Masho SW, Adera T, Ramakrishnan V, Roberts JD. Association between family history of prostate cancer. JMH. 2010;7:45-54.
23. Rosai J, Ackerman's. Prostate. In: Rosai, Ackerman, editors. Surgical Pathology, Vol 2 ($10^{th}$ edition). New Delhi: Mosby. 2011;585-855.
24. Aronson WJ, Barnard RJ, Freedland SJ, Henning S, Elashoff D, Jardack PM, Cohen P, et al. Growth inhibitory effect of low fat diet on prostate cancer cells: results of a prospective, randomized dietary intervention trial in men with prostate cancer. J Urol. 2010;183:345-350
25. Gibson TM, Ferrucci LM, Tangrea JA, Schatzkin A. Epidemiological and clinical studies of nutrition. Semin Oncol. 2010;37:282-296.
26. Rohrmann S, Platz EA, Kavanaugh CJ, Thuita L, Hoffman SC, Helzlsouer KJ. Meat and dairy consumption and subsequent risk of prostate cancer in a US cohort study. Cancer Causes Control. 2007;18:41-50
27. Giovannucci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC. A prospective study of cruciferous vegetables and prostate cancer. Cancer Epidemiol Biomarkers Prev. 2003;12:1403-1409

28. Handayani R, Rice L, Cui Y, Medrano TA, Samedi VG, Baker HV, Szabo NJ, et al. Soy isoflavones alter expression of genes associated with cancer progression, including interleukin-8, in androgen-independent PC-3 human prostate cancer cells. J Nutr. 2006;136:75-82.
29. de Vogel S, Meyer K, Fredriksen A, Ulvik A, Ueland PM, Nygard O, Vollset SE, et al. Serum folate and vitamin B12 concentrations in relation to prostate cancer risk—a Norwegian population-based nested case-control study of 3000 cases and 3000 controls within the JANUS cohort. Int J Epidemiol. 2013;42:201-210.
30. Fuentes E, Fuentes F, Vilahur G, Badimon L, Palomo I. Mechanisms of chronic state of inflammation as mediators that link obese adipose tissue and metabolic syndrome. Mediators Inflamm. 2013; 2013:136584.
31. Gurel B, Lucia MS, Thompson IM, Jr., Goodman PJ, Tangen CM, Kristal AR, Parnes HL, et al. Chronic inflammation in benign prostate tissue is associated with highgrade prostate cancer in the placebo arm of the prostate cancer prevention trial. Cancer Epidemiol Biomarkers. Prev. 2014;23:847-856
32. Taylor ML, Mainous AG, 3rd, Wells BJ. Prostate cancer and sexually transmitted diseases: a meta-analysis. Fam Med. 2005;37:506-512.
33. Prashanth Rawla. Epidemiology of Prostate Cancer. World J Oncol. 2019;10:63-89.
34. Hamilton W, Sharp D. J, Peters T. J, Round A. P, Clinical features of prostate cancer before diagnosis: a population-based, case-control study. Br J Gen Pract. 2006; 56: 756–762.

35. Buyyounouski M K, Choyke PL,. McKenney J K, Sartor O, Sandler HM, Amin MB etal. Prostate Cancer – Major Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual. CA CANCER J CLIN 2017;67:245–253.
36. Lee H , Lee M , Byun S. S , Lee S. E , Hong S. K . Evaluation of Prostate Cancer Stage Groups Updated in the 8th Edition of the American Joint Committee on Cancer Tumor-Node-Metastasis Staging Manual. Clin Genitourin Cancer 2019 ;17:221-226
37. Humphrey P. A, Moch. H, Cubilla A. L , Ulbright. T.M , Reuter V. E. The 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs-Part B: Prostate and Bladder Tumours. Eur Urol 2016 ;70:106-119
38. Asmarinah A, Paradowska-Dogan A, Kodariah R, Tanuhardja B, Waliszewski P, Mochtar CA et al. Expression of Bcl2 family genes and complexes in mitochondrial transport in prostate cancer cells. Int J Oncol 2014;45:1489-1496
39. Anwari A, Toussi MS, Kalantari M et al. Expression of Bcl2 and Bax gene in Advanced or Metastatic prostate carcinoma. Urology Journal 2012;09:381-387
40. Rubial A, Aguiar P, Rio MC et al. Positive immunohistochemical expression of bcl2 in hormone independent breast carcinomas is associated with a greater lymph node involvement and poor outcome. Medical Oncology Journal 2014;31:1-4.
41. . Mirakhor S, Samani, Bojnordi TE, Zarghampour M et al. Expression of p53, Bcl-2 and Bax in endometrial carcinoma, endometrial hyperplasia and normal endometrium: a histopathologiacal study. Journal of Obstetrics and Gynaecology [Internet]. 2018, Mar; Available from: https://doi.org/10.1080/01443615.2018.1437717

42. Gaffney C , Liu D, Cooley V, Ma X , Angulo C ,Robinson B etal. Tumor size and genomic risk in localized prostate cancer. Urologic Oncology: Seminars and Original Investigations. 2021; 39: 434
43. Tolonen TT, Tommola S, Jokinen S, Parviainen T, Martikainen PM. Bax and Bcl-2 are focally overexpressed in the normal epithelium of cancerous prostates. Scand J Urol Nephrol. 2007;41:85-90.
44. Amirghofran Z, Monabati A, Gholijani N. Apoptosis in prostate cancer: bax correlation with stage. Int J Urol. 2005;12:340-5.
45. Lacopino F, Angelucci C, Lama G, et al. Apoptosis-related gene expression in benign prostatic hyperplasia and prostate carcinoma. Anticancer Res. 2006;26:1849-54.
46. Hering FL, Lipay MV, Lipay MA, Rodrigues PR, Nesralah LJ, Srougi M. Comparison of positivity frequency of bcl-2 expression in prostate adenocarcinoma with low and high Gleason score. Sao Paulo Med J. 2001;119:138-41.
47. Gupta S, Gupta A, Saini AK, Majumder K, Sinha K, Chahal A. Prostate Cancer: How Young is too Young? Curr Urol [Internet]. 2017;9(4):212–5. Available from: http://dx.doi.org/10.1159/000447143
48. Yamamoto S, Senzaki A, Yamagiwa K, Tanaka T, Oda T. Prostatic carcinoma in a young adult: a case report. Hinyokika Kiyo. 1990;36:617–622.
49. Roberts JT, Essenhigh DM. Adenocarcinoma of prostate in 40-year-old body-builder. Lancet. 1986;2(8509):742.
50. Davis BE, Weigel JW. Adenocarcinoma of the prostate discovered in 2 young patients following total prostatovesiculectomy for refractory prostatitis. J Urol. 1990;144:744–745.

51. Desai MM, Cacciamani GE, Gill K, Zhang J, Liu L, Abreu A, et al. Trends in incidence of metastatic prostate cancer in the US. JAMA Netw Open [Internet]. 2022;5(3):e222246. Available from: http://dx.doi.org/10.1001/jamanetworkopen.2022.2246
52. Friedersdorff F, Groß B, Maxeiner A, Jung K, Miller K, Stephan C, et al. Does the Prostate Health Index depend on tumor volume?-A study on 196 patients after radical prostatectomy. Int J Mol Sci [Internet]. 2017;18(3):488. Available from: http://dx.doi.org/10.3390/ijms18030488
53. Alshahmi E, Obida E, Emaetig F, Elgaraboli F, Alqawi O. The Expression Profile of Bcl-2 Protein in Prostate Cancer Patients. Clin Oncol. 2021;6:1833
54. Khor L-Y, Desilvio M, Li R, McDonnell TJ, Hammond MEH, Sause WT, et al. Bcl-2 and bax expression and prostate cancer outcome in men treated with radiotherapy in Radiation Therapy Oncology Group protocol 86-10. Int J Radiat Oncol Biol Phys [Internet]. 2006;66(1):25–30. Available from: http://dx.doi.org/10.1016/j.ijrobp.2006.03.056
55. Krajewska M, Krajewski S, Epstein JI, Shabaik A, Sauvageot J, Song K, et al. Immunohistochemical analysis of bcl-2, bax, bcl-X, and mcl-1 expression in prostate cancers. Am J Pathol. 1996;148(5):1567–76.
56. Yoshino T, Shiina H, Urakami S, Kikuno N, Yoneda T, Shigeno K, et al. Bcl-2 expression as a predictive marker of hormone-refractory prostate cancer treated with taxane-based chemotherapy. Clin Cancer Res [Internet]. 2006;12(20 Pt 1):6116–24. Available from: http://dx.doi.org/10.1158/1078-0432.CCR-06-0147

57. Aihara M, Lebovitz RM, Wheeler TM, Kinner BM, Ohori M, Scardino PT. Prostate specific antigen and gleason grade: an immunohistochemical study of prostate cancer. J Urol [Internet]. 1994;151(6):1558–64. Available from: http://dx.doi.org/10.1016/s0022-5347(17)35302-8

# ANNEXURES

## INFORMED CONSENT FORM

**STUDY TITLE: EXPRESSION OF Bcl2 AND Bax GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORING.**

I, _____have read or have been read to me the patient information sheet and understand the purpose of the study, the procedure that will be used, the risk and benefits associated with my involvement in the study and the nature of

information will be collected and disclosed during the study.

I have had my opportunity to ask my questions regarding various aspects of the study and my questions are answered to my satisfaction.

I, the undersigned, agree to participate in this study and authorize the collection and disclosure of my personal information for the dissertation.

Name and signature / thumb impression Date:

(subject) Place:

Name and signature / thumb impression Date:

Place:

(Witness/Parent/ Guardian/ Husband)

# PATIENT PROFORMA SHEET

**STUDY TITLE: EXPRESSION OF Bcl2 AND Bax GENE IN PROSTATE CARCINOMA AND ITS CORRELATION WITH GLEASON SCORING**.

PLACE OF STUDY: Sri Devaraj Urs Medical College attached to R.L Jalappa Hospital and Research,Tamaka, Kolar.

The main aim of the study is to study the expression of Bcl2 and Bax gene in prostate carcinoma and its correlation with gleason scoring.

You are requested to participate in a study conducted by the department of pathology as a part of dissertation. This study will be done on prostate carcinoma specimens of the patients. The specimens will be collected from the department of pathology, SDUMC,Kolar.

This study will be approved by the institutional ethical committee. The information collected will be used only for dissertation and publication. There is no compulsion to agree to participate. You are requested to sign / provide thumb impression only if you voluntarily agree to participate in the study.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. You will not receive any monetary benefits to participate in this research.

This informed consent document is intended to give you a general background of study.Please read the following information carefully and discuss with your family members. You can ask your queries related to study at any time during the study.

If you are willing to participate in the study you will be asked to sign an informed consent form by whichyou are acknowledging that you wish to participate in the study and entire procedure will be explained to you by the study doctor. You are free to withdraw your consent to participate in the study any time without explanation and this will not change your future care

For any clarification you are free to contact the investigator.

PRINCIPAL INVESTIGATOR : Dr. AYSWARIA

ಮಾಹಿತಿ ಸಮ್ಮತಿ ನಮೂನೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ: Bcl2 ಮತ್ತು Bax ನ ಅಭಿವ್ಯಕ್ತಿ ಜೀನ್ ಪ್ರೊಸ್ಟೇಟ್ ಕಾರ್ಸಿನೋಮ ಮತ್ತು ಗ್ಲೀಸನ್ ಸ್ಕೋರಿಂಗ್ನಿಂದಿಗೆ ಅದರ ಪರಸಪರ ಸಂಬಂಧ.

ನಾನು, _____ ರೀಗಿ ಮಾಹಿತಿ ಹಾಳೆಯನು ಓದಿದ್ದೀನೆ ಮತ್ತು ಅಧ್ಯಯನದ ಉದ್ದೀಶವನು ಅರ್ಿಮಾಡಿ, ಬಳಸಲಾಗುವ ಕಾಯಿವಿಧಾನ, ಅಧ್ಯಯನದಲ್ಲಿ ನನು ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಮತ್ತು ನನು ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಗೆ ಸಂಬಂಧಿಸಿದ ಅಪಾಯ ಮತ್ತು ಪ್ರಯೀಜನಗಳ್ಳ

ಮತ್ತು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಮಾಹಿತಿಯನು ಸಂಗರಹಿಸಲಾಗುತ್ುದ್ ಮತ್ತು ಬಹಿರಂಗಪ್ಡಿಸಲಾಗುತ್ುದ್.

ಅಧ್ಯಯನದ ವಿವಿಧ್ ಆಯಾಮಗಳ ಬಗೊ ನನು ಪ್ರಶ್ನಗಳನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶ ದೊರೆತಿತ್ತು ಮತ್ತು ನನು ಪ್ರಶ್ನಗಳಿಗೆ ನನು ತೃಪ್ತುಗೆ ಉತ್ುರಿಸಲಾಗಿದ್.

ನಾನು, ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಮತ್ತು ನನು ವೈಯಕ್ತುಕ ಮಾಹಿತಿಯನು ಸಂಗರಹಿಸುವುದು ಮತ್ತು ಬಹಿರಂಗಪ್ಡಿಸುವಿಕೆಯನು ಈ ಲೇಖನಕಾಾಗಿ ಅಧಿಕೃತ್ಗೊಳಿಸಲು ನಾನು ಒಪ್ಪುತ್ುೀನೆ.

ಹೆಸರು ಮತ್ತು ಸಹಿ / ಹೆಬ್ಬೆಟ್ಟು ಗುರುತ್ತ ದಿನಾಾಂಕ:

ಸಥಳ:

ಹೆಸರು ಮತ್ತು ಸಹಿ / ಹೆಬ್ಬೆಟ್ಟು ಗುರುತ್ತ ದಿನಾಾಂಕ:

ಸಥಳ:

(ಸಾಕ್ಷಿ/ಪೀಷಕ/ ಪಾಲಕ/ ಪ್ತಿ)

ರೀಗಿ ಮಾಹಿತಿ ಸಮಮತಿ ನಮೂನೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ: ಪರಸ್ುೀಟ್ ಕಾಸಿಿನೀಮಾದಲ್ಲಿ Bcl2 ಮತ್ತು Bax ಜೀನ್ ನ ಅಭಿವಯಕ್ತು ಮತ್ತು ಗೆಿಸನ್ ಸ್ಾಿೀರಿಾಂಗ್ ನಾಂದಿಗೆ ಅದರ ಸಂಬಂಧ್.

ಸಥಳ: ಆರ್.ಎಲ್.ಜಾಲಪ್ು ಆಸುತ್ರ ಮತ್ತು ಸಂಶೀಧ್ನಾ ಕೇಾಂದರ ಕೀಲಾರಕೌ ಹಾಂದಿಕಾಂಡಿರುವ ಶರೀ ದೇವರಾಜ ಅರಸು ವೈದಯಕ್ತೀಯ ಕಾಲೇಜು.

ಪಾರಸ್ುೀಟ್ ಕಾಸಿಿನೀಮಾದಲ್ಲಿ Bcl2 ಮತ್ತು Bax ಜೀನ್ ನ ಅಭಿವಯಕ್ತು ಮತ್ತು ಗೆಿಸನ್ ಸ್ಾಿೀರಿಾಂಗ್ ನಾಂದಿಗಿನ ಅದರ ಸಂಬಂಧ್ವನುು ಅಧ್ಯಯನ ಮಾಡುವುದು ಅಧ್ಯಯನದ ಮುಖಯ ಉದ್ದೀಶವಾಗಿದ್.

ನೀವು ರೀಗಶಾಸುರ ವಿಭಾಗವು ನಡೆಸಿದ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವಂತ್ ನಮಮನುು ವಿನಂತಿಸಲಾಗಿದ್. ಈ ಅಧ್ಯಯನವನುು ರೀಗಿಗಳ ಪಾರಸ್ುೀಟ್ ಕಾಸಿಿನೀಮಾ ಮಾದರಿಗಳ ಮೇಲೆ ಮಾಡಲಾಗುತ್ುದ್. ಮಾದರಿಗಳನುು ರೀಗಶಾಸುರ ವಿಭಾಗ, ಎಸ್ ಡಿಯುಎಾಂಸಿ,ಕೀಲಾರದಿಾಂದ ಸಂಗರಹಿಸಲಾಗುವುದು.

ಈ ಅಧ್ಯಯನವನುು ಸಾಾಂಸಿಥಕ ನೈತಿಕ ಸಮಿತಿ ಯು ಅನುಮೀದಿಸುತ್ುದ್. ಸಂಗರಹಿಸಿದ ಮಾಹಿತಿಯನುು ಕೇವಲ ಲೇಖನ ಮತ್ತು ಪ್ರಕಟಣೆಗಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ುದ್. ಇದರಲ್ಲಿ ಭಾಗವಹಿಸಲು ಯಾವುದೇ ಒತ್ತುಯವಿಲಿ. ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸವಇಚ್ಛೆಯಾಂದ ಒಪ್ತುಕಾಂಡರೆ ಮಾತ್ರ ನೀವು ಸಹಿ ಮಾಡಲು / ಹೆಬ್ಬೆಟ್ಟುನ ಗುರುತ್ನುು ನೀಡಲು ವಿನಂತಿಸಲಾಗುತ್ುದ್.

ನಮಿಮಾಂದ ಸಂಗರಹಿಸಿದ ಎಲಾಿ ಮಾಹಿತಿಯನುು ಗೌಪ್ಯವಾಗಿಇಡಲಾಗುತ್ುದ್ ಮತ್ತು ಯಾವುದೇ ಹರಗಿನವರಿಗೆ ಬಹಿರಂಗಪ್ಡಿಸಲಾಗುವುದಿಲಿ. ನಮಮ ಗುರುತ್ನುು ಬಹಿರಂಗಪ್ಡಿಸುವುದಿಲಿ. ಈ ಸಂಶೀಧ್ನೆಯಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಮಗೆ ಯಾವುದೇ ಆರ್ಥಿಕ ಪ್ರಯೀಜನಗಳ್ಳ ದೊರೆಯುವುದಿಲಿ.ಈ ಮಾಹಿತಿಯುತ್ ಸಮಮತಿ ದಸಾುವೇಜು ನಮಗೆ ಅಧ್ಯಯನದ ಸಾಮಾನಯ ಹಿನೆಲೆಯನುು ನೀಡುವ ಉದ್ದೀಶವನುು ಹಾಂದಿದ್. ದಯವಿಟ್ಟು

ಈ ಕೆಳಗಿನ ಮಾಹಿತಿಯನು ಎಚ್ಚರಿಕೆಯಾಂದ ಓದಿ ಮತ್ತು ನಮಮ ಕುಟ್ಟಾಂಬ ಸದಸಯರಾಂದಿಗೆ ಚ್ಚೆಸಿ. ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನಕೆಾ ಸಂಬಂಧಿಸಿದ ನಮಮ ಪ್ರಶ್ನಗಳನು ನೀವು ಕೇಳಬಹುದು.ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸಿದಧರಿದದರೆ, ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಬಯಸುವ ು ದಾಗಿ ನೀವು ಒಪ್ತುಕಾಂಡಿರುವ ಮಾಹಿತಿಯುತ್ ಸಮಮತಿ ನಮೂನೆಗೆ ಸಹಿ ಮಾಡುವಂತ್ ನಮಮನು ಕೇಳಲಾಗುತ್ುದ್ ಮತ್ತು ಇಡೀ ಕಾಯಿವಿಧಾನವನು ಅಧ್ಯಯನ ವೈದಯರು ನಮಗೆ ವಿವರಿಸುತ್ತುರೆ. ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ವಿವರಣೆ ಇಲಿದ್ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಮಮ ಸಮಮತಿಯನು ಹಿಾಂತ್ಗೆದುಕಳುಲು ನೀವು ಸವತಂತ್ರರಿದಿದೀರಿ ಮತ್ತು ಇದು ನಮಮ ಭವಿಷಯದ ಆರೈಕೆಯನು ಬದಲ್ಲಸುವುದಿಲಿ.ಯಾವುದೇ ಸುಹುನೆಗಾಗಿ ನೀವು ತ್ನಖಾಧಿಕಾರಿಯನು ಸಂಪ್ಕ್ತಿಸಲು ಸವತಂತ್ರರು.ಮುಖಯ ಪ್ರಿಶೀಧ್ಕ : ಡಾ. ಐಸಾವರಿಯಾ

# PATIENT PROFORMA

Name :

Age: Hospital Number:

**Anonymised Sample No:**

**Chief complaint :**

**History of presenting illness :**

**Past history :**

**Personal history :**

**Local examination:**

**Clinical TNM staging :**

**Biopsy Number:**

**Histopathological diagnosis :**

**Gross :**

**Microscopy :**

**Gleasons score:**

**Stage of disease:**

# MASTER CHART

# KEY TO MASTER CHART

PSA-Prostate specific Antigen

MRI/CT-Magnetic Resonance Imaging/Computed tomography

| S.NO | BIOPSY NO | AGE | UHID NO | DIAGNOSIS | GLEASON SCORE | GLEASON GRADE | Clinical symptoms | PSA levels | MRI/CT TUMOR SIZE | METASTASIS | CLINICAL STAGING | H-SCORE BCL2 | H SCORE BAX | | FOLLOW UP |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | B-1891-16 | 79 | 307474 | ADENOCARCINOMA PROSTATE | 4+5 | Grade 5 | **Urinary retention** | 60 | 7.2X6X5 | PRESENT | T4 | 220 | 100 | | on treatment |
| 2 | B-2717-16 | 68 | 340786 | ADENOCARCINOMA PROSTATE | 5+4 | Grade 5 | **Urinary hestitation & dribbling** | 69 | 3.1X 2X4 | PRESENT | T3 | 180 | 90 | | expired at 3 months |
| 3 | B-2719-16 | 70 | 344620 | ADENOCARCINOMA PROSTATE | 4+4 | Grade 4 | **Burning micturition** | 75 | 5.5X6X2.1 | PRESENT | T3 | 220 | 90 | | on treatment |
| 4 | B-331-17 | 67 | 390741 | PROSTATE ADENOCARCINOMA | 3+4 | Grade 2 | **Urinary hestitation & dribbling** | 25 | 3.3X2.5X3 | PRESENT | T3 | 160 | 110 | | expired on 6 months follow up |
| 5 | B-420-17 | 44 | 400794 | PROSTATE ADENOCARCINOMA | 5+3 | Grade 4 | **Urinary retention** | 78 | 6X3X3 | PRESENT | T3 | 190 | 80 | | expired at 7 months |
| 6 | B-1811-17 | 75 | 463449 | ADENOCARCINOMA PROSTATE | 5+4 | Grade 5 | **Burning micturition** | 91 | 7.4X6.7X5 | PRESENT | T3 | 250 | 130 | | on treatment |
| 7 | B-1928-17 | 58 | 468082 | ADENOCARCINOMA PROSTATE | 5+4 | Grade 5 | **Burning micturition** | 82 | 7.4x6x5 | PRESENT | T4 | 170 | 115 | | on treatment |
| 8 | B-459-18 | 73 | 552521 | ADENOCARCINOMA PROSTATE | 3+4 | Grade 2 | **Urinary hestitation & dribbling** | 9 | 2.5x2x2 | NOT PRESENT | T2 | 150 | 80 | | expired at 9 months |
| 9 | B-1392-18 | 65 | 590889 | PROSTATE ADENOCARCINOMA | 4+3 | Grade 3 | **Urinary retention** | 31 | 4.3x3x2.5 | PRESENT | T3 | 130 | 90 | | on treatment |
| 10 | B-1571-18 | 80 | 596575 | PROSTATE ADENOCARCINOMA | 5+5 | Grade 5 | **Urinary hestitation & dribbling** | 69 | 7.5x8x6 | PRESENT | T4 | 240 | 125 | | on treatment |
| 11 | B-2255-18 | 82 | 627884 | ADENOCARCINOMA PROSTATE | 4+5 | Grade 5 | **Urinary retention** | 90 | 3x2.4x2 | PRESENT | T4 | 150 | 75 | | on treatment |
| 12 | B-3021-18 | 77 | 663128 | PROSTATE ADENOCARCINOMA | 5+4 | Grade 5 | **Burning micturition** | 32 | 7.8x6.2x5.2 | PRESENT | T3 | 200 | 115 | | expired at 12 months |
| 13 | B-723-19 | 65 | 699647 | ADENOCARCINOMA PROSTATE | 5+5 | Grade 5 | **Burning micturition** | 90 | 8x5x4.5 | PRESENT | T3 | 190 | 95 | | on treatment |
| 14 | B-1174-19 | 68 | 721829 | ADENOCARCINOMA PROSTATE | 4+5 | Grade 5 | **Urinary hestitation & dribbling** | 65 | 6.5x4.7x3.6 | PRESENT | T4 | 210 | 110 | | on treatment |
| 15 | B-1399-19 | 80 | 724005 | ADENOCARCINOMA PROSTATE | 4+4 | Grade 4 | **Urinary hestitation & dribbling** | 106 | 9.2x7x8.8 | PRESENT | T3 | 180 | 90 | | on treatment |
| 16 | B-1452-19 | 65 | 728111 | PROSTATE ADENOCARCINOMA | 5+5 | Grade 5 | **Urinary hestitation & dribbling** | 110 | 8x5.5x3 | PRESENT | T4 | 180 | 140 | | no details available |
| 17 | B-1115-19 | 65 | 736247 | ADENOCARCINOMA PROSTATE | 5+5 | Grade 5 | **Urinary retention** | 50 | 5.5x4.2x3 | PRESENT | T3 | 200 | 90 | | no details available |
| 18 | B-2141-19 | 80 | 750389 | PROSTATE ADENOCARCINOMA | 4+5 | Grade 5 | **Burning micturition** | 44 | 6x5x5 | PRESENT | T3 | 170 | 100 | | on treatment |
| 19 | B-2802-19 | 71 | 651468 | ADENOCARCINOMA PROSTATE | 5+5 | Grade 5 | **Urinary retention** | 77 | 7.5x6x5 | PRESENT | T4 | 190 | 100 | | on treatment |
| 20 | B-599-19 | 65 | 688865 | ADENOCARCINOMA PROSTATE | 5+5 | Grade 5 | **Burning micturition** | 46 | 5.5x4x4 | PRESENT | T4 | 240 | 125 | | expired at 5 months |
| 21 | B-1388-19 | 67 | 729116 | ADENOCARCINOMA PROSTATE | 5+4 | Grade 5 | **Burning micturition** | 54 | 6.7x4.2x3.2 | PRESENT | T4 | 210 | 80 | | on treatment |
| 22 | B-269-20 | 75 | 818677 | PROSTATE ADENOCARCINOMA | 2+3 | Grade 1 | **Urinary retention** | 7 | 5.2x3.5x2.2 | NOT PRESENT | T2 | 170 | 75 | | on treatment |
| 23 | B-1253-20 | 60 | 856973 | PROSTATE ADENOCARCINOMA | 4+3 | Grade 3 | **Urinary hestitation & dribbling** | 10 | 2.2x2x1.5 | NOT PRESENT | T2 | 190 | 85 | | no details available |
| 24 | B-54-21 | 65 | 887098 | PROSTATE ADENOCARCINOMA | 3+4 | Grade 2 | **Urinary retention** | 31.6 | 5.5x4x2.5 | PRESENT | T2 | 200 | 130 | | on treatment |
| 25 | B-125-21 | 65 | 886479 | PROSTATE ADENOCARCINOMA | 3+4 | Grade 2 | **Burning micturition** | 107 | 7.5x4.1x3.6 | PRESENT | T3 | 190 | 90 | | on treatment |
| 26 | B-353-21 | 68 | 897465 | POORLY DIFFERENTIATED ADENOCARCINOMA PROSTATE | 4+4 | Grade 4 | **Urinary hestitation & dribbling** | 75 | 7.7x5.4x6 | PRESENT | T4 | 110 | 90 | | on treatment |
| 27 | B-867-21 | 66 | 920608 | PROSTATIC ADENOCARCINOMA | 5+4 | Grade 5 | **Burning micturition** | 50 | 5.5X4.2X2.3 | PRESENT | T3 | 250 | 90 | | no details available |
| 28 | B-1044-21 | 90 | 928490 | PROSTATIC ADENOCARCINOMA | 4+3 | Grade 3 | **Urinary hestitation & dribbling** | 28 | 8x8x7 | PRESENT | T4 | 120 | 85 | | on treatment |
| 29 | B-1099-21 | 80 | 929746 | PROSTATIC ADENOCARCINOMA | 4+4 | Grade 4 | **Urinary retention** | 58 | 2.2x3x2 | NOT PRESENT | T2 | 230 | 140 | | on treatment |
| 30 | B-1174-21 | 75 | 930532 | PROSTATIC ADENOCARCINOMA | 3+4 | Grade 2 | **Urinary retention** | 10 | 2x2x2 | NOT PRESENT | T2 | 210 | 100 | | on treatment |
| 31 | B-814-21 | 65 | 920806 | PROSTATIC ADENOCARCINOMA | 5+4 | Grade 5 | **Burning micturition** | 91 | 7.4x6.7x5 | PRESENT | T4 | 220 | 80 | | no details available |
| 32 | B-978-16 | 83 | 275494 | PROSTATIC ADENOCARCINOMA | 3+3 | Grade 2 | **Burning micturition** | 6 | 3.7X4X3.3 | NOT PRESENT | T2 | 120 | 60 | | expired at 8 months |
| 33 | B-2517-17 | 75 | 505938 | PROSTATIC ADENOCARCINOMA | 3+3 | Grade 2 | **Urinary hestitation & dribbling** | 120 | 8X4.6X5.6 | PRESENT | T2 | 200 | 120 | | on treatment |
| 34 | B-619-19 | 55 | 697122 | PROSTATIC ADENOCARCINOMA | 3+4 | Grade 2 | **Urinary retention** | 18 | 4.2x4x3 | PRESENT | T3 | 180 | 100 | | on treatment |

| S.NO | BIOPSY NO | AGE | UHID NO | DIAGNOSIS | GLEASON SCORE | GLEASON GRADE | Clinical symptoms | PSA levels | MRI/CT TUMOR SIZE | METASTASIS | CLINICAL STAGING | H-SCORE BCL2 | H SCORE BAX | | FOLLOW UP |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 35 | B-1615-19 | 65 | 736247 | PROSTATIC ADENOCARCINOMA | 5+5 | Grade 5 | **Urinary retention** | 46 | 5.5X4X4 | PRESENT | T4 | 160 | 90 | | on treatment |
| 36 | B-654-16 | 40 | 261525 | PROSTATIC ADENOCARCINOMA | 5+5 | Grade 5 | **Urinary hestitation & dribbling** | 71 | 5X4.5X4 | PRESENT | T4 | 150 | 80 | | no details available |
| 37 | B-1203-16 | 71 | 283731 | PROSTATIC ADENOCARCINOMA | 3+4 | Grade 2 | **Urinary hestitation & dribbling** | 29 | 5X4.2X3 | NOT PRESENT | T2 | 190 | 70 | | on treatment |
| 38 | B-1110-18 | 80 | 577423 | PROSTATIC ADENOCARCINOMA | 3+3 | Grade 2 | **Burning micturition** | 9 | 3.5X4X2 | NOT PRESENT | T2 | 100 | 80 | | on treatment |
| 39 | B-1135-18 | 75 | 579136 | PROSTATIC ADENOCARCINOMA | 4+3 | Grade 3 | **Burning micturition** | 22 | 5.5X4X4 | PRESENT | T3 | 130 | 90 | | expired at 9 months |
| 40 | B-1854-19 | 70 | 746780 | PROSTATIC ADENOCARCINOMA | 5+5 | Grade 5 | **Urinary retention** | 55 | 3X2.5X4 | PRESENT | T4 | 220 | 180 | | on treatment |
| 41 | B-1967-16 | 70 | 305802 | PROSTATIC ADENOCARCINOMA | 3+5 | Grade 4 | **Urinary hestitation & dribbling** | 25 | 4.9X5X3 | PRESENT | T3 | 180 | 110 | | on treatment |
| 42 | B-1998-19 | 82 | 752890 | PROSTATIC ADENOCARCINOMA | 4+5 | Grade 5 | **Urinary retention** | 59 | 8X9X8 | PRESENT | T3 | 190 | 95 | | no details availbale |
| 43 | B-2023-16 | 70 | 311958 | PROSTATIC ADENOCARCINOMA | 3+5 | Grade 4 | **Urinary hestitation & dribbling** | 44 | 3.5X3.8X2 | PRESENT | T2 | 140 | 85 | | on treatment |
| 44 | B-2837-18 | 77 | 307474 | PROSTATIC ADENOCARCINOMA | 5+5 | Grade 5 | **Burning micturition** | 83 | 8X4.5X6 | PRESENT | T4 | 240 | 170 | | on treatment |
| 45 | B-310-18 | 74 | 538882 | PROSTATIC ADENOCARCINOMA | 4+3 | Grade 3 | **Burning micturition** | 35 | 3.2X4X3 | PRESENT | T2 | 195 | 100 | | on treatment |
| 46 | B-646-20 | 60 | 838031 | PROSTATIC ADENOCARCINOMA | 4+5 | Grade 5 | **Urinary retention** | 85 | 7.5x4x3.3 | PRESENT | T3 | 210 | 140 | | on treatment |
| 47 | B-1392-19 | 65 | 590889 | PROSTATIC ADENOCARCINOMA | 4+3 | Grade 3 | **Urinary hestitation & dribbling** | 25 | 4.5X4X3 | PRESENT | T2 | 170 | 90 | | on treatment |
| 48 | B-25-21 | 65 | 887220 | PROSTATIC ADENOCARCINOMA | 3+3 | Grade 3 | **Urinary retention** | 52 | 3X2.5X1.5 | NOT PRESENT | T2 | 130 | 100 | | on treatment |
| 49 | B-1835-22 | 70 | 945680 | PROSTATIC ADENOCARCINOMA | 4+4 | Grade 4 | **Burning micturition** | 109 | 2.5X1X1 | NOT PRESENT | T2 | 160 | 120 | | on treatment |
| 50 | B-92-22 | 74 | 845632 | PROSTATIC ADENOCARCINOMA | 4+5 | Grade 5 | **Urinary hestitation & dribbling** | 69 | 7.8X6.2X5.2 | PRESENT | T3 | 200 | 140 | | on treatment |