"THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN 1(CD 138) AND ITS CORRELATION WITH STAGING AND GRADING OF COLORECTAL CARCINOMA"

BY

Dr. SUDARSHAN K, **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 OF MEDICINE

IN

PATHOLOGY

UNDER THE GUIDANCE OF

Dr. HEMALATHA A, *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

"THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN 1(CD 138) AND ITS CORRELATION WITH STAGING AND GRADING OF COLORECTAL CARCINOMA"

IN SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR

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

Dr. HEMALATHA A

PROFESSOR,

DEPARTMENT OF PATHOLOGY,

SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR

DATE: SIGNATURE OF THE CANDIDATE

PLACE: KOLAR Dr. SUDARSHAN K

CERTIFICATE BY THE GUIDE

THIS IS TO CERTIFY THAT THE DISSERTATION ENTITLED

"THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN-1(CD 138) AND ITS CORRELATION WITH STAGING AND GRADING OF COLORECTAL CARCINOMA"AT R.L. JALAPPA HOSPITAL AND RESEARCH CENTRE, KOLAR

IS A BONAFIDE RESEARCH WORK

DONEBY

Dr. SUDARSHAN K

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

M.D IN PATHOLOGY

DATE:

SIGNATURE OF THE GUIDE

PLACE: KOLAR

Dr. HEMALATHA A, MD
PROFESSOR
DEPARTMENT OF PATHOLOGY

CERTIFICATE BY THE CO-GUIDE

THIS IS TO CERTIFY THAT THE DISSERTATION ENTITLED

"THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN-1 (CD 138) AND ITS CORRELATION WITH STAGING AND GRADING OF COLORECTAL CARCINOMA"AT R.L. JALAPPA HOSPITAL AND RESEARCH CENTRE, KOLAR

IS A BONAFIDE RESEARCH WORK DONE

BY

Dr. SUDARSHAN K

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

M.D IN PATHOLOGY

DATE:

PLACE: KOLAR

SIGNATURE OF THE CO- GUIDE

Dr. KRISHNA PRASAD

PROFESSOR & HOD
DEPARTMENT OF SURGERY

ENDORSEMENT BY THE HOD,PRINCIPAL/HEADOF THE INSTITUTION

THIS IS TO CERTIFY THAT THE DISSERTATION ENTITLED

"THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN 1(CD 138) AND ITS CORRELATION WITH STAGING AND GRADING OF COLORECTAL CARCINOMA"

IS A BONAFIDE RESEARCH WORK DONE BY

Dr. SUDARSHAN K

UNDER THE GUIDANCE OF

DR. HEMALATHA A, ***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

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

DISSEMINATETHIS DISSERTATION,

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

DATE

PLACE: KOLAR

SIGNATURE OF THE CANDIDATE

Dr. SUDARSHAN K

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR.

ETHICS COMMITTEE

CERTIFICATE

THIS IS TO CERTIFY THAT, THE ETHICS COMMITTEE OF

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA,

KOLARHAS UNANIMOUSLY APPROVED

Dr. SUDARSHAN K

POST GRADUATE STUDENT IN THE DEPARTMENT OF

PATHOLOGY OFSRI DEVARAJ URS MEDICAL COLLEGE

TO TAKE UP THE DISSERTATION WORK ENTITLED

"THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN 1(CD 138) AND ITS CORRELATION WITH STAGING AND GRADING OF COLORECTAL CARCINOMA"

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/ 566(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 " **The Immunohistochemical Expression of Syndecan-1 (CD 138) and its Correlation with staging and Grading of colorectal carcinoma"** being investigated by **Dr.Sudarshan K,** Dr.Hemalatha A & Dr. Krishna Prasad[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 Committe
Sri Devaraj Urs Medical Coll
Tamaka, Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH

Tamaka, Kolar 563103

Certificate of Plagiarism Check

Title of the Thesis/Dissertation	THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN-1 (CD-138) AND ITS CORRELATION WITH STAGING AND GRADING OF COLORECTAL CARCINOMA
Name of the Student	Dr. SUDARSHAN K
Registration Number	20PA1002
Name of the Supervisor / Guide	Dr. HEMALATHA A
Department	PATHOLOGY
Acceptable Maximum Limit (%) of Similarity (PG Dissertation /Ph.D. Thesis)	10%
Similarity	6 %
Software used	Turnitin
Paper ID	1991157044
Submission Date	11/01/2023

Signature of Student

11.1.23

Signature of Guide/Supervisor

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

11/01/23

HOD Signature

Professor And HOD
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 Devaraj Urs Medical College ,
Tamaka, Kolar- 563103

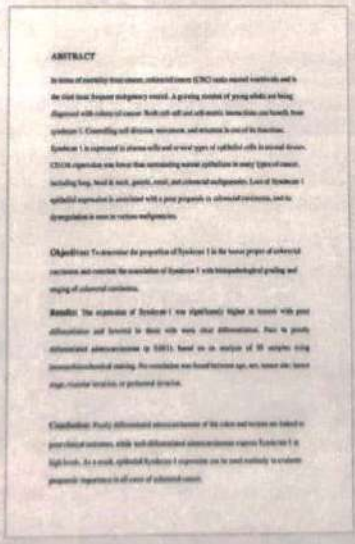
turnitin

Digital Receipt

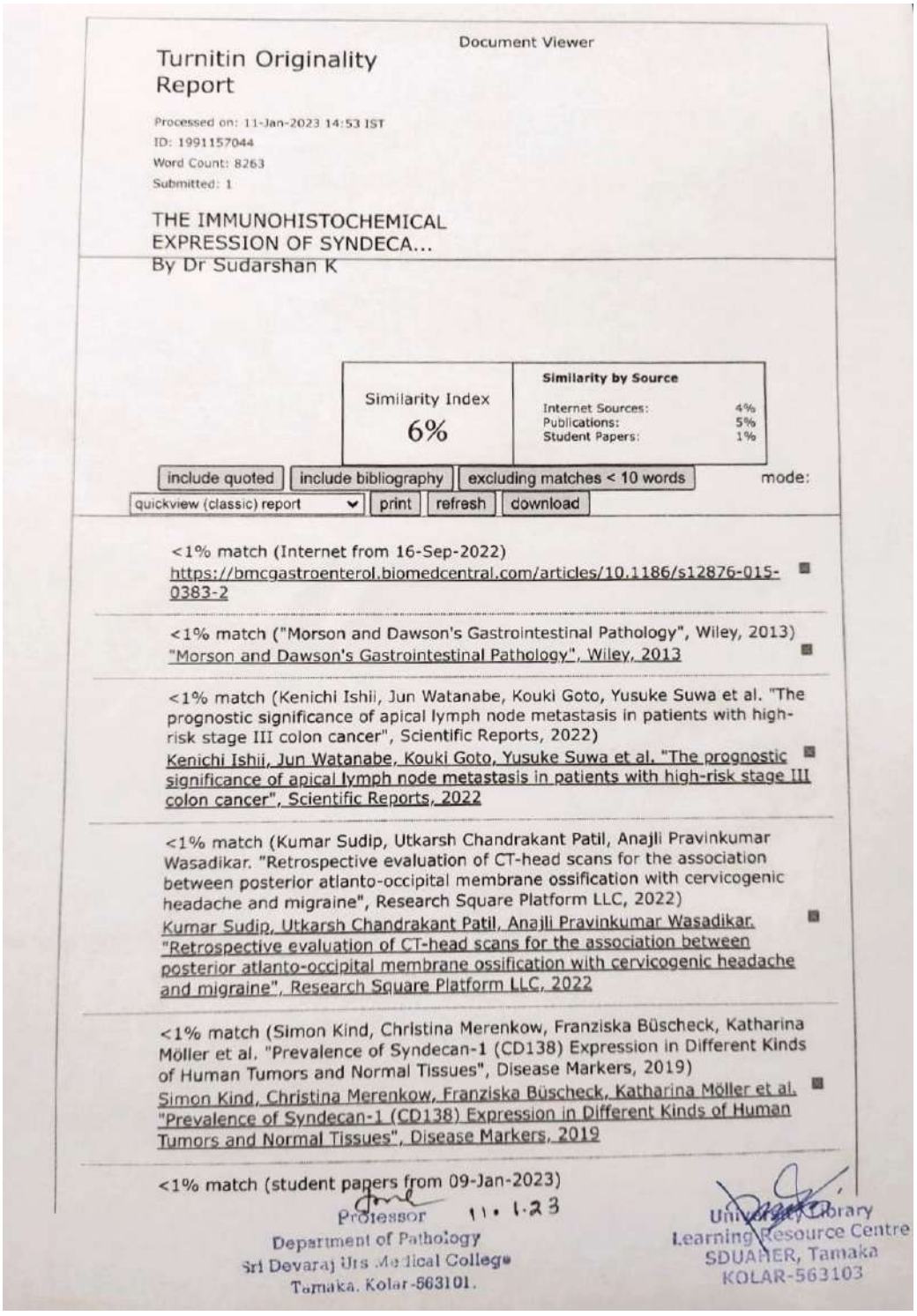
This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	Dr Sudarshan K
Assignment title:	Thesis
Submission title:	THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECAN 1(...
File name:	ORRELATION_WITH_STAGING_AND_GRADING_OF_COLORECT...
File size:	17.32M
Page count:	58
Word count:	8,263
Character count:	45,695
Submission date:	11-Jan-2023 02:52PM (UTC+0530)
Submission ID:	1991157044



ABSTRACT



Document Viewer

Turnitin Originality Report

Processed on: 11-Jan-2023 14:53 IST
ID: 1991157044
Word Count: 8263
Submitted: 1

THE IMMUNOHISTOCHEMICAL EXPRESSION OF SYNDECA...
By Dr Sudarshan K

Similarity Index	Similarity by Source	
6%	Internet Sources:	4%
	Publications:	5%
	Student Papers:	1%

include quoted | include bibliography | excluding matches < 10 words | mode:
quickview (classic) report | print | refresh | download

<1% match (Internet from 16-Sep-2022)
https://bmcgastroenterol.biomedcentral.com/articles/10.1186/s12876-015-0383-2

<1% match ("Morson and Dawson's Gastrointestinal Pathology", Wiley, 2013)
"Morson and Dawson's Gastrointestinal Pathology", Wiley, 2013

<1% match (Kenichi Ishii, Jun Watanabe, Kouki Goto, Yusuke Suwa et al. "The prognostic significance of apical lymph node metastasis in patients with high-risk stage III colon cancer", Scientific Reports, 2022)
Kenichi Ishii, Jun Watanabe, Kouki Goto, Yusuke Suwa et al. "The prognostic significance of apical lymph node metastasis in patients with high-risk stage III colon cancer", Scientific Reports, 2022

<1% match (Kumar Sudip, Utkarsh Chandrakant Patil, Anajli Pravinkumar Wasadikar. "Retrospective evaluation of CT-head scans for the association between posterior atlanto-occipital membrane ossification with cervicogenic headache and migraine", Research Square Platform LLC, 2022)
Kumar Sudip, Utkarsh Chandrakant Patil, Anajli Pravinkumar Wasadikar. "Retrospective evaluation of CT-head scans for the association between posterior atlanto-occipital membrane ossification with cervicogenic headache and migraine", Research Square Platform LLC, 2022

<1% match (Simon Kind, Christina Merenkow, Franziska Büscheck, Katharina Möller et al. "Prevalence of Syndecan-1 (CD138) Expression in Different Kinds of Human Tumors and Normal Tissues", Disease Markers, 2019)
Simon Kind, Christina Merenkow, Franziska Büscheck, Katharina Möller et al. "Prevalence of Syndecan-1 (CD138) Expression in Different Kinds of Human Tumors and Normal Tissues", Disease Markers, 2019

<1% match (student papers from 09-Jan-2023)

Professor 11.1.23
Department of Pathology
Sri Devaraj Urs Medical College
Tamaka, Kolar-563101.

University Library
Learning Resource Centre
SDUAHER, Tamaka
KOLAR-563103

ACKNOWLEDGEMENT

I begin by expressing my immense gratitude to the almighty lord for his blessings.

My continued reverence and acknowledgement to my beloved teacher and guide ***Dr. HEMALATHA A****, Professor of Pathology, who graced the study officially with her constant support and expert advice, her encouragement, wise constructive judgement the painstaking effort to weed out errors and her affection during course of study leaves me permanently indebted to her. I dedicate the good part of the work to her*

I take this opportunity to express my humble and sincere gratitude and indebtedness to my 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. M.L. HARENDRA KUMAR,*** *Professor ,for his constant guidance, support and encouragement and for handpicking the current topic for me.*

I express my sincere and humble gratitude to ***Dr. T.N. Suresh****, Professor, for his support, constructive advice and constant encouragement.*

I express my deep immense gratitude and humble thanks to ***Dr. Subhasish Das****, Professor, for his advice and encouragement throughout the study.*

I would like to convey my sincere thanks to ***Dr. Manjula K*** *professors, for their constant support throughout the course.*

I wish to express my sense of gratitude to ***Dr. Swaroop Raj B V****,*

Associate Professor, for his kind help and expert advice in preparing this dissertation.

I express my sincere thanks to ***Dr. Shilpa M D, Dr. Supreetha M S,*** *Associate Professors, for their constant guidance and encouragement in preparing this dissertation.*

I express my sincere thanks to ***Dr. Sindhi C, Dr. B. Haritha,*** *Assistant Professors, for their constant guidance and encouragement in preparing this dissertation.*

I express my sincere thanks to my parents, ***Mr. Mr. R. Krishnappa and Mrs. R. Nagalakshmi*** *my brother* ***Mr. K. Janardhan****, who have and will always be my biggest source of strength and inspiration for their unconditional love and support in every aspect of my life, I am forever indebted.*

I express my sincere thanks to my batchmates and friends, ***Dr. Vajja Nagaraju****,* ***Dr. Amrutha, Dr. Snigdha, Dr. Ankita, Dr. Satadruti, Dr. Aishwariya*** *for their support and love in every aspect of my life.*

My immense gratitude and special thanks to my seniors and friends, ***Dr. Priyanka, Dr. Ankith, Dr. Gaurav, Dr. Sonia*** *for their support and love. I thank them for their kind co-operation.*

I enjoyed working with my juniors ***Dr. Priyanka DVS, Dr. Ambika, Dr. Divya, Dr. Queen, Dr. Zubiya, Dr. Sahiti, Dr. Deepika, Dr. Manju Alex, Dr. Kamala, Dr. Sarjubala, Dr. Prathiba, Dr. Nikita, Dr. Bhadra, Dr. Deepa, and Dr. Nikita****. I thank them for their kind cooperation.*

I am thankful to ***Dr. Chetan*** *for his guidance in statistics.*

I am thankful to technical staff ***Mr Veerendra, Ms Sumathi, Ms Asha, Mr.Shankar, Mr.Ananthu, Mr. Muthuraya swamy*** *and all non-teaching staff* ***Mr. Partha , Mr****.* ***Jayaram*** *and also blood bank 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. Sudarshan k***

LIST OF ABBREVATIONS

CRC- Colo Rectal Carcinoma

APR- Abdomino-Perineal Resection

H&E- Hematoxylin and Eosin

HPF- High Power Fields

IHC- Immuno Histo Chemistry

AJCC- American Joint Committee on Cancer

ABSTRACT

BACKGROUND: In terms of mortality from cancer, colorectal cancer (CRC) ranks second and is the third most frequent malignancy worldwide. Syndecan-1 acts in both cell-cell and cell-matrix interactions. Controlling cell division, movement, and structure of the cell is one of its functions. Syndecan-1 expression was lower than surrounding normal epithelium in many types of malignancies and loss of its expression is associated with a poor prognosis in various malignancies.

AIMS & OBJECTIVES: To determine the proportion of Syndecan 1 in the tumor proper of colorectal carcinoma and its association with histopathological grading and staging.

MATERIALS AND METHODS: 95 colorectal cancer cases that underwent surgical resection in total were examined. All cases' H & E slides were examined, and immunohistochemistry was run against Syndecan-1. IHC expression levels were assessed, divided into groups based on high and low expression, and these values were compared to clinicopathological information about the cases, including age, sex, histological grading, lymph node status, and staging. IBM SPSS Statistics, Somers, NY, USA. Software was used in determining p value.

RESULTS: Based on 95 samples, Syndecan-1 expression was significantly low in tumours with poor differentiation and increased in well-differentiated CRCs and statistically significant with CRC malignancy grading (p 0.001). No correlation was found between age, sex, tumour site, tumour stage, vascular invasion, or perineural invasion.

CONCLUSION: Poorly differentiated colon and rectum adenocarcinomas express little Syndecan-1, but well-differentiated ones do. Thus, epithelial Syndecan-1 expression can be employed in all colorectal cancer cases to assess prognosis.

KEYWORDS: Colorectal carcinoma, Syndecan-1, Prognosis of CRCs

TABLE OF CONTENTS

LIST OF TABLES

LIST OF CHARTS

LIST OF FIGURES

INTRODUCTION

INTRODUCTION

One of the most common malignancies to be discovered is colorectal carcinoma (CRC), which also has a high mortality rate among cancer patients. Still, the risk of developing CRCs sporadically in Asian populations is low to minimal.[1,2]

Numerous factors act at the molecular level, like DNA mismatch repair, microsatellite repeat regions, Mutations in the oncogenes KRAS and SMAD2 and SMAD4 as well as environmental variables all play critical roles in the progression to malignant colorectal tumours. CRCs are more common among the aged 60-70 years. Various other factors are considered risk factors for developing CRCs, including polyps, adenomas, diet (red meat, animal fat, alcohol), sedentary lifestyle, obesity, and positive family history. It is a slow-growing tumor and may remain asymptomatic for years.[3]

The tumor, nodes, and metastasis staging (TNM) give the prognosis of CRCs. The American Joint committee on cancer recommends additional prognostic factors that should be determined and reported to indicate the prognosis of CRCs.[4,5]

Among the recommended parameters for CRC prognosis are serum carcinoembryonic antigen (CEA) levels, lymph nodes showing tumor cells within the area of its lymphatic drainage, and vascular and neural invasion, which shows a poorer prognosis.[5]

Multiple novel markers have emerged as important in determining CRC prognosis, according to recent studies. Syndecan-1 is one such marker; it facilitates communication between cells and between cells and their surrounding matrix. Syndecan-1 contributes to the regulation of cell division, migration, and morphology. Plasma cells and other

epithelial cell types in normal tissues express Syndecan-1.[6]

Expression of Syndecan-1 over the epithelial surface is deregulated in several cancers, while loss of its epithelial expression shows a bad prognosis in colorectal carcinoma. Evaluation of Syndecan-1 by immunohistochemistry allows the identification of changing patterns of its expression which is involved in the progression and differentiation of the CRCs.[7,8]

AIMS & OBJECTIVES

OBJECTIVES OF THE STUDY

1. To determine the proportion of Syndecan 1 in the tumor proper of colorectal carcinoma
2. To correlate the association of Syndecan 1 with histopathological grading and staging of colorectal carcinoma.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

EMBRYOLOGY OF LARGE INTESTINE.[9,10]

The primitive tube, which forms the foregut, midgut, and hindgut, includes the intestines from its posterior part. A relatively straight cylindrical primitive tube transforms into a folded complex of tubes that forms the characteristic adult intestinal tract.

The superior mesenteric artery, which comes from the aorta, sends blood through this tube to the midgut. Midgut forms the caecum & appendix. Along with continuation from caecum ascending colon, and most of the transverse colon are formed.

Around the sixth week of life inside the womb, the midgut loop forms. By the tenth week, it connects to the omphalomesenteric duct.

The midgut loop has a cranial and caudal limb, and mesentery suspends these loops in the abdominal cavity. The cranial loop multiplies and forms the intestinal loops. The caudal loops include the caecal swelling, which appears in the ante mesenteric border of the midgut loop, which further grows slowly in the apex, forming an appendix.

The remaining portion of the large intestine is the hindgut, which comprises of the left side of one-third of the transverse colon up to the anal canal and is fed by the inferior mesenteric artery. The cloaca that forms at the end of the hindgut contributes to the formation of the anal canal and rectum.

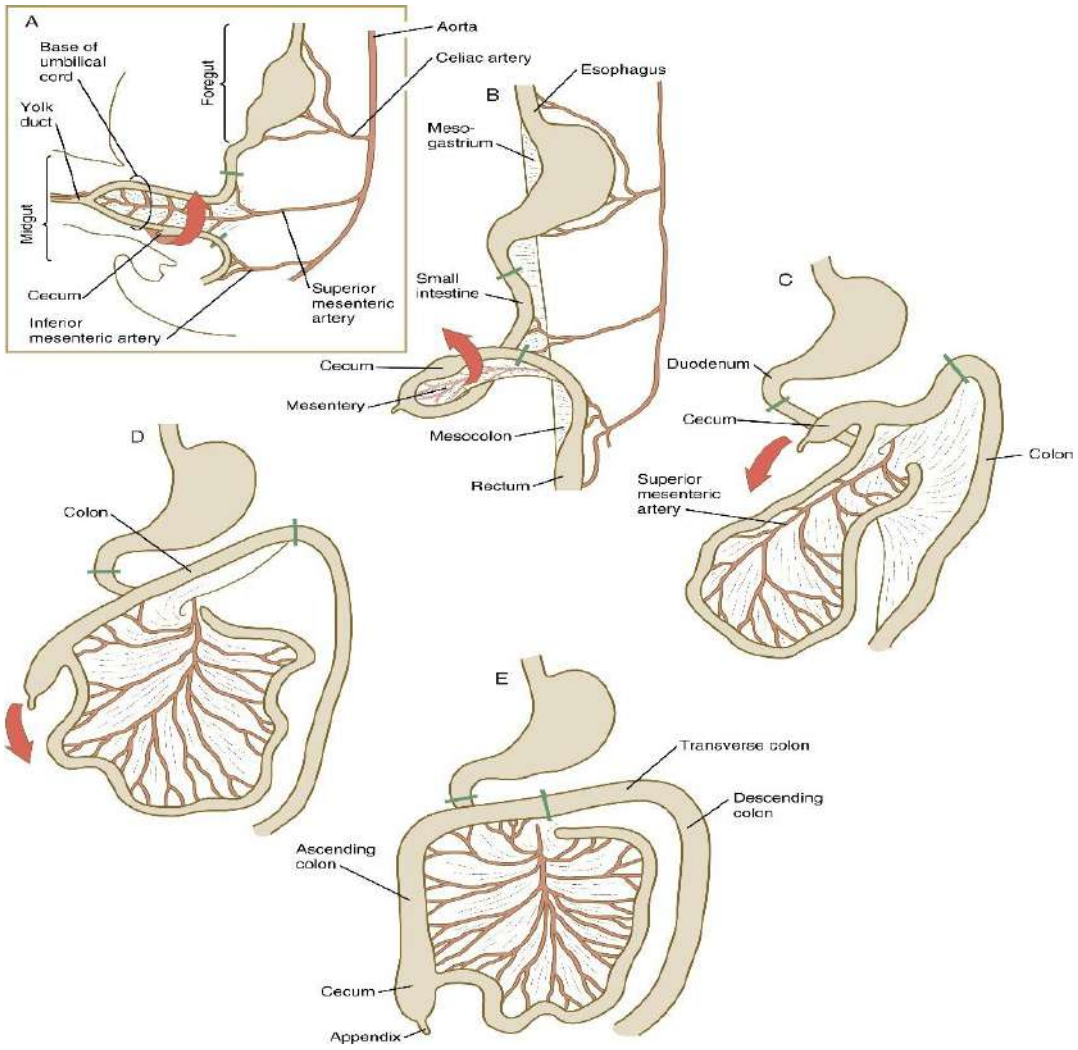


Figure 1. The stages of large intestine development and its rotation. (A) the fifth week of development. (B) the sixth week of intrauterine life. (C) the eleventh week of intrauterine life. (D) twelfth week of intrauterine life. (E) after twelve weeks of intrauterine life. (Image from Human Embryology and Developmental Biology Sixth Edition.[9])

Anatomy of the large intestine[11,12]

Colon starts from ileocecal junction and extends till anus. Colon begins in right iliac fossa and ascends superiorly in the lateral region till right hypochondriac region where it turns to left forming right colic flexure and continues as transverse colon. To produce the left colic flexure, the muscle twists to the left and curls on the abdomen's left side. At this point, the colon descends to form the descending colon, continues as the sigmoid colon in the pelvis, and transforms into the rectum, which is located at the level of the third sacral vertebrae in the smaller pelvis. At the level of the pelvic diaphragm, the rectus muscle forms the anal canal.

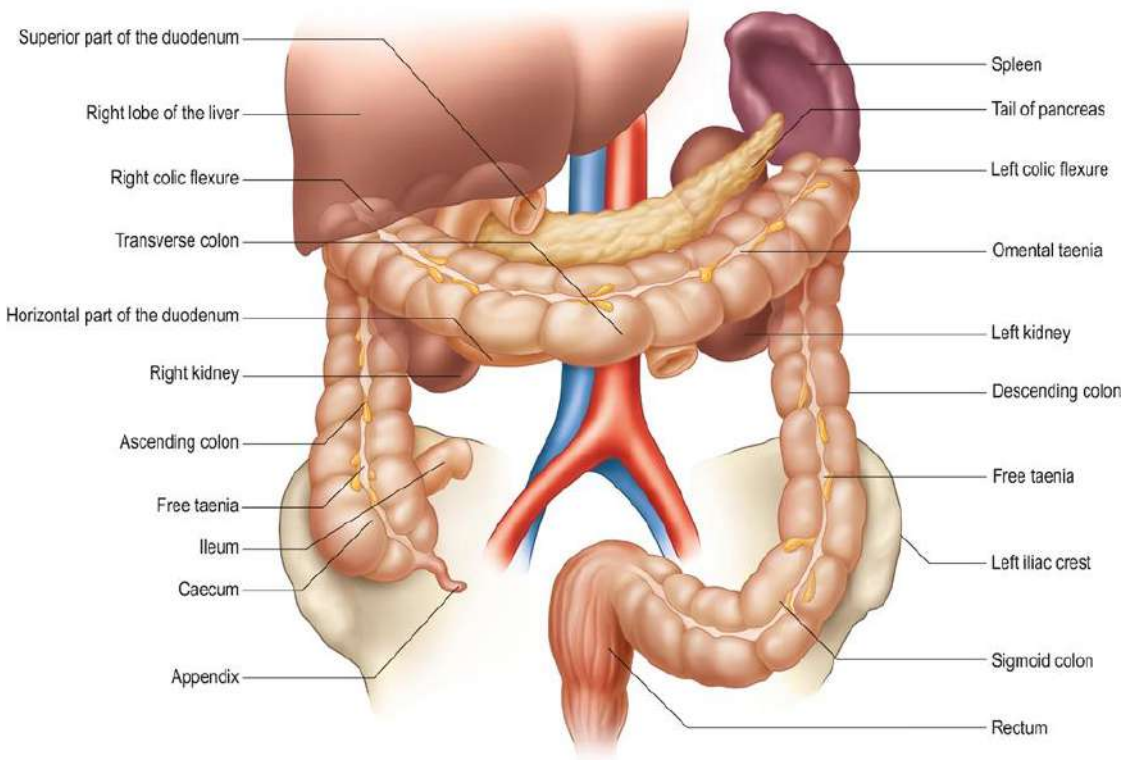


Figure 2. Large intestine in abdominal cavity (Image from Gray's Anatomy. 42nd edition[11])

HISTOLOGY OF LARGE INTESTINE [14, 15]

The large intestine generally has four separate layers histologically, with minor alterations, like other regions of the alimentary canal. The simple to tall columnar epithelium that lines the large intestine digs into the surface to a depth of about 0.5 mm, creating crypts in the mucosa. The lining of the colon has a large number of goblet cells. The cellular lamina propria lies beneath the mucosal layer and may contain lymphoid clusters. Lamina propria is followed by the submucosa and muscularis propria. There is a significant amount of fully developed adipose tissue in the submucosa. The muscularis propria refers to the smooth muscle cells present in the colon. The large intestine is innervated by Meissner's plexus, which is between the submucosal layer and muscularis propria, and Auerbach's plexus, which lies between the layers of muscularis propria. Both the ascending and descending colon has adventitia due to its presence in retroperitoneal. The mesentery, which contains the remainder of the colon is enclosed by serosa. With a few of the following exceptions, the rectum and colon are comparable to one another. The rectum lacks taenia, lacks appendices epiploicae, has a continuous longitudinal muscle coat, and has serous layer covering on its lateral sides in the upper third of the rectum.

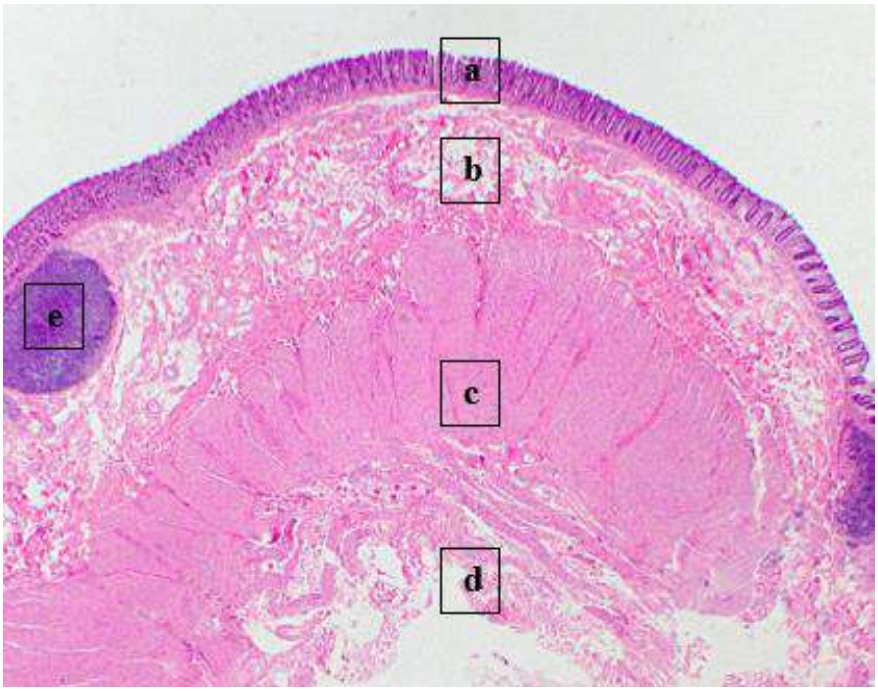


Figure 3. Histological layers of the colon (a) mucosa (b) submucosa (c) muscularis propria (d) serosa (e) lymphoid aggregates in submucosal layer (Image from Pathology Outlines – Anatomy & histology[13])

Large intestines lymphatic drainage[11]

Large intestine lymphatic drainage occurs after mesenteric artery blood flow. The result is that the superior mesenteric lymph nodes get lymph nodes from the ascending colon, the proximal section of the transverse colon, and the caecum. The lymph nodes that border the path of the inferior mesenteric artery drain the distal portion of the transverse colon until rectum.

Epidemiology of colorectal cancer[14–16]

CRCs are linked to a high rate of morbidity and deaths across North America and Europe, as well as the areas with similar dietary practices and lifestyles to those described above.

CRCs account for 10% of malignancies which indicates it to be the third most common cancer next to breast and lung cancers accounting for 11.7% and 11.4% of overall cancers diagnosed and its related deaths worldwide.

In the year 2020, nearly 1.93 million of the newly diagnosed CRCs and around 0.9 million of CRC related deaths were registered. Incidence of CRC was 19.5 per million of CRC cases which include 23.4 per million in males and 16.2 per million in females. Mortality related to CRC was 9 per million of worldwide population in 2020. Highest incidence of mortality was seen in Northern European zone accounting for 33.6 per million and South-Central Asia with 5.5 per million as second highest rate for CRC related deaths.

CRC was among the fifth most common cancer of incidence in India, with record of 65358 newly diagnosed cases in 2020. Rate of incidence in Indian population was 4.8 per million and mortality rate was 2.8 per million.

In India, colorectal cancer is fifth among all cancers in incidence, accounting for 65358 new cases (40408 in males, 24950 in females) in 2020. The incidence rate is 4.8 per 100,000, and the mortality rate is 2.8 per 100,000 in India.

Risk factors for development of colorectal carcinoma[14,16]

Increased Risk (Convincing or Probable Evidence)

- Intake of alcohol above 30 g per day
- Processed meat and meats preserved by smoking and adding up of chemicals for preservation
- Increased BMI

Increased Risk (Limited suggestive evidence)

- Tobacco smoking
- Mutagens and carcinogens in environment
- Foods that has heme iron
- Charbroiled and fried meat or fish which contain heterocyclic amines
- Reduced intake of fruits
- Inadequate intake of non-starchy vegetables
- Dysbiosis of intestinal microbiota

Decreased Risk (Convincing or probable evidence)

- Usage of drugs like calcium supplements, NSAIDs, Aspirin, COX-2 inhibitors and Oestrogen used in hormonal replacement therapy
- Consumption of dairy products
- Foods rich in fibers and whole grains
- Low body mass and physical activity

Decreased Risk (Limited suggestive evidence)

- Vitamin C and Vitamin D
- Fish
- Multivitamin supplements

Genetics of colorectal cancers.[16]

Many genetic factors are known to be involved in the development of CRCs, some of them are as follows,

- RAS gene mutations seen in over >50% of full-blown CRCs.
- Chromosome 17p deletion at TP53 region occurs in >75% cases.
- Chromosome 5 allele loss seen in 70 % of cases.
- 18q deletion seen in 50-70% cases of CRCs with invasion
- SMAD2 & SMAD4 deletions
- Loss of DCC gene in overt CRCs
- Accumulation of RAS and TP53 gene mutations, LOH on 5q & 18q mutations seen during the transition from benign adenoma to carcinomas
- CRC shows two to more of the above-mentioned alterations in 90% cases

Pathogenesis of colorectal carcinoma[3]

Colonic adenocarcinoma develops due to epigenetic and genetic alterations which are heterogenous molecular changes. Most important mechanisms in development of CRCs are activation of APC/β-catenin seen in transition of classic adenoma to carcinoma, and the association of repeated microsatellite regions caused by DNA mismatch repair mechanisms.

APC/β-catenin pathway and DNA mismatch repair pathway occurs in a stepwise manner which causes several mutations that involve multiple genes. Epigenetic event in progression of both the pathways is methylation-induced gene silencing.

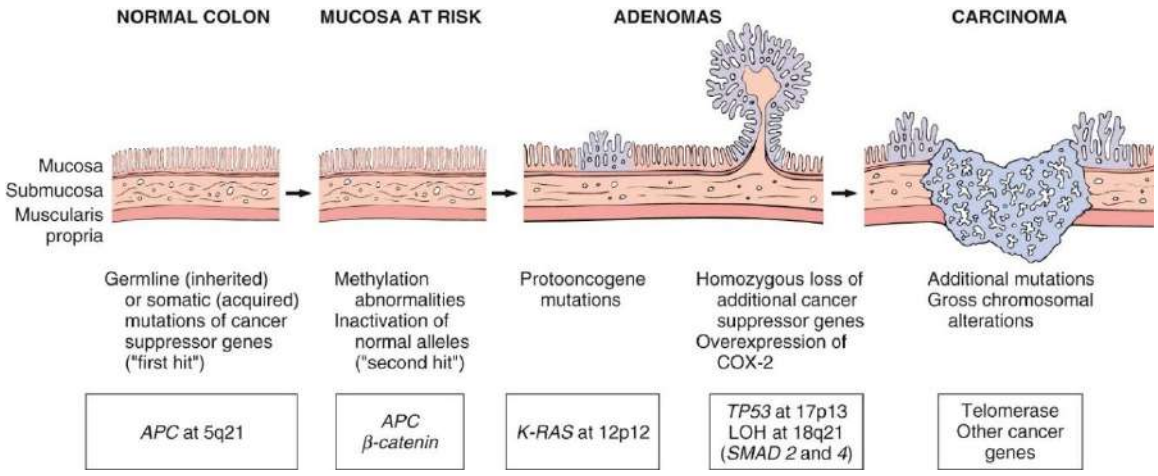


Figure 4. Progression of normal colon to adenomas and carcinomas through genetic alteration (Image taken form Robbins & Cotran Pathologic basis of the disease, 10th edition[3])

Transition of classic adenomas into carcinomas occurs in nearly 80% of the cases. Inactivation of both alleles of APC gene is necessary for development of adenomas. Due to the loss of APC gene, β-catenin and TCF which are essential DNA-binding factors form a complex which promotes cell proliferation by activation MYC and cyclin D1 transcription.

In few cases there is KRAS mutations seen among tumors with <1cm size. In adenomas which are >1cm in size, KRAS mutations are seen in nearly 50% cases.

Tumor suppressor genes like SMAD2 and SMAD4 which affects TGF-β signaling is also known to cause CRCs by unrestricted cell growth and cell cycle inhibition.

CRCs show mutation in TP53 gene in form of chromosomal instability and chromosomal deletions. This causes instability of APC/β-catenin pathway that act as a tumor suppressor. Along with this methylation of CpG-rich zones, CpG islands and 5' regions which are promoter and transcriptional start sites that help in cell differentiation is mutated. Telomerase expression is increased in cases with advanced disease.

Loss of BAX gene which helps in survival of mutated clones is seen in progressive CRCs.

Overall mutations in BRAF, MSI instability and methylation of MLH1 forms the carcinogenic pathway is a well-established phenomenon in CRCs.

Clinical features in colorectal carcinoma[17,18]

CRC symptoms might manifest as sharp abdominal pain or as nonspecific, long-lasting symptoms. Anemia, which is a symptom of colon cancer on the right side, causes anemia-related symptoms like weakness, dullness, and decreased activity. Tumor on the left side of the colon presents with bleeding and tenesmus. Very rarely mass per abdomen will be the constitutional symptom in CRCs. Rarely hematuria and infection in urinary tract due to fistula in urinary bladder or fistula in gastrocolic region causing severe diarrhea.

Symptoms of the CRCs are non-specific. Stratification of patients as high-risk category for urgent investigations is based on the symptoms of changed bowel habits, mass per rectum and chronic anemia. Accordingly high-risk and low-risk symptoms are as follows

Higher risk

- Rectal bleed
- Consistent rectal bleeding without soreness, discomfort, itching, lumps, prolapse, or pain.
- Changes in bowel habits, such as hard stools or increased frequency of passing stools, that last for six weeks in individuals of all ages. (> 60 years)
- Right-sided abdominal lump that can be felt (all ages)
- Rectal lump that can be felt (not pelvic) (all ages)
- Unexplained anemia due to a lack of iron (all ages)

Low risk

- People who are not anemic
- Rectal bleeding with an evident external origin, such as anal fissure
- No lump per abdomen or rectum (all ages)
- Rectal bleeding with no evident change in bowel habits.
- Temporary changes in bowel habits brought on by passing firmer stools or less frequent urination
- Intestinal discomfort without blockage (all ages)

WHO HISTOLOGICAL CLASSIFICATION OF TUMORS OF THE COLON AND RECTUM[4]

BENIGN EPITHELIAL TUMOURS AND PRECURSORS:

Serrated dysplasia, low grade

Serrated dysplasia, high grade

Hyperplastic polyp, micro vesicular type

Hyperplastic polyp, goblet cell

Adenomatous polyp, low-grade dysplasia

Adenomatous polyp, high-grade dysplasia

Tubular adenoma, low grade

Tubular adenoma, high grade

Villous adenoma, low grade

Villous adenoma, high grade

Tubulovillous adenoma, low grade

Tubulovillous adenoma, high grade

Advanced adenoma

Glandular intraepithelial neoplasia, low grade

Glandular intraepithelial neoplasia, high grade

MALIGNANT EPITHELIAL TUMOURS:

Adenocarcinoma NOS

Serrated adenocarcinoma

Adenoma like adenocarcinoma

Micropapillary adenocarcinoma

Mucinous adenocarcinoma

Poorly cohesive carcinoma

Signet ring cell carcinoma

Medullary adenocarcinoma

Adenosquamous carcinoma

Carcinoma undifferentiated, NOS

Carcinoma with sarcomatoid component

Neuroendocrine tumors

Neuroendocrine tumor, grade 1

Neuroendocrine tumor, grade 2

Neuroendocrine tumor, grade 3

L cell tumor

Glucagon-like peptide-producing tumor PP/PYY-producing tumor Enterochromaffin –

cell carcinoid Serotonin-producing tumor

Neuroendocrine carcinoma NOS

Large cell neuroendocrine carcinoma

Small cell neuroendocrine carcinoma

Mixed neuroendocrine–non–neuroendocrine neoplasm (MiNEN)

COMMON COLORECTAL NEOPLASMS[19]

EPITHELIAL POLYPS

The majority of the colorectal polyps are those with epithelial genesis. Adenomatous polyps and serrated polyps are two major types into which they can be categorized. Juvenile (retention) polyp is the most frequent colonic polyp seen in children.

TUBULAR ADENOMA

Adenomatous polyps, sometimes referred to as tubular adenomas, are typically evenly distributed throughout the entire large intestine but less frequently in the rectum. These are typically asymptomatic and occasionally lead to changes in bowel habits. They can be sessile or pedunculated and are typically smaller than 1 cm in size. These adenomas are composed of tubular crypts that are closely spaced apart and only include 20% villous tissue. These exhibit cellular crowding and glandular hyperplasia, as well as possible abnormal nuclear characteristics. Increased positive is seen when Carcino embryonic antigen (CEA) expression is immunostained, especially in the atypical parts.

VILLOUS ADENOMA

These are frequently solitary and seen in older age range. Rectum and recto sigmoid areas are the most frequent sites, although due to the lesions' extremely soft consistency, even a digital inspection often misses them. More than 80% of the components in these adenomas are villous. They have a broad base from which finger-like villi emerge. Long papillary structures and a crown-like pattern may be visible under a light microscope. Treatment

varies depending on the size and severity of the lesion. A 29%–70% chance of malignant transformation exists.

SERRATED ADENOMA

These are typically sessile and tiny, not exceeding 5 mm. These adenomas are known as serrated because they exhibit saw-toothed architecture under a microscope. These are distinctive and consist of the glands folding into the lumen. Additional mitotic activity might be observed. Sessile, conventional, and hyperplastic serrated adenomas are the three types of serrated adenomas.

TUBULO VILLOUS ADENOMA

These often combine villous and tubular elements, with 20–80% of the villous element present.

Syndromes associated with colorectal carcinomas are Familial adenomatous polyposis (FAP; also known as polyposis coli), Gardner syndrome, Turcot syndrome and Cowden syndrome.

ADENOCARCINOMA

The tumour cells must completely penetrate the muscularis mucosae into the submucosa in order to be classified as a carcinoma.. They are usually asymptomatic; the most common presentation mode is a change in bowel habits, haematochezia, or anemia. Colonoscopy may aid in the early diagnosis. The growth pattern may be exophytic with intraluminal growth,

diffusely infiltrative/ linitis plastic type with endophytic change, or with complete circumferential involvement.

MUCINOUS CARCINOMA

Malignant cells with more than 50% extracellular mucin pools. Usually associated with microsatellite instability.

SIGNET RING CELL CARCINOMA

The cells should have eccentrically placed nuclei with intracellular mucin, and the cells should comprise more than 50 % of tumor cells.

ADENOSQUAMOUS CARCINOMA

The entity should contain a combination of squamous cell carcinoma and adenocarcinoma elements. There should be more than one component and convincing foci of squamous cell carcinoma.

MEDULLARY CARCINOMA

It is a rare tumor with a reasonably good prognosis and characterized by a solid pattern of cells with a vesicular nucleus, prominent nucleoli, and eosinophilic cytoplasm.

TNM CLASSIFICATION OF COLORECTAL TUMORS[4]

Tumor	Regional lymph nodes	Distant metastasis
Tx- Primary tumor cannot be assessed	Nx- regional lymph nodes cannot be assessed	M0- no distant metastasis
T0- no evidence of primary tumor	N0- no regional lymph node metastasis	M1- distant metastasis to one or more sites or organs or peritoneal metastasis
Tis- carcinoma insitu, intramucosal carcinoma	N1- metastasis to one to three regional lymph nodes	M1a- metastasis to one site or organ without peritoneal metastasis
T1- tumor invades the submucosa	N1a- metastasis in one regional lymph node	M1b- metastasis to two or more sites or organs without peritoneal metastasis
T2- tumor invades the muscularis propria	N1b- metastasis in two or three regional lymph nodes	M1c- metastasis to peritoneal surface, alone or with other site or organ metastasis
T3- tumor invades through the muscularis propria into peri colorectal tissues	N1c- tumor deposits in subserosa or in non-peritonealised pericolic or perirectal soft tissue without regional nodal metastasis	
T4- tumor invades visceral peritoneum or invades or adheres to adjacent organ	N2- metastasis in four or more regional lymph nodes	
T4a- tumor invades visceral peritoneum		
T4b- tumor invades or adheres to adjacent organs		

Table 1: TNM classification of colorectal carcinomas

Stage 0	Tis	N0	M0
Stage I	T1, T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T1, T2	N1/ N1c	M0
Stage IIIA	T1	N2a	M0
Stage IIIB	T3-T4a	N1/ N1c	M0
Stage IIIB	T2, T3	N2a	M0
Stage IIIB	T1, T2	N2b	M0
Stage IIIC	T4a	N2a	M0
Stage IIIC	T3-T4a	N2b	M0
Stage IIIC	T4b	N1-N2	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b
Stage IVC	Any T	Any N	M1c

Table 2: TNM staging of colorectal carcinoma.

MOLECULAR CLASSIFICATION OF COLORECTAL CARCINOMAS[20]

Due to heterogenous molecular constituents in development of CRCs a single molecular classification for colorectal carcinomas is not prepared. Based on the proliferation index and tumor differentiation and survival rates associated with their expression CRCs can be classified into four groups.

Molecular classes	Driving role of biomarkers	Median survival in months
CRC Novel Class-1	Low Ki67, high CDX2 & low P53	30
CRC Novel Class-2	High ki67, low CDX2 & low P 53	25
CRC Novel Class-4	High ki67, high CDX-2 & high P53	26
CRC Novel Class-4	High ki67, high CDX-2 & low P53	23

Table 3: Molecular classification of colorectal carcinomas.

PROGNOSTIC FACTORS IN COLORECTAL CARCINOMA.[21–43]

Factors associated with bad prognosis or poor outcomes are

- Stage of presentation
- Post treatment stage of carcinoma
- Depth of penetration of the tumor
- Local involvement of peritoneum
- Tumor size >4.5 cm
- Presence of tumor after definitive therapy
- The circumferential margin (CRM) and presence of tumor cell at ≤1mm from CRM and the point of deepest penetration
- The presence of tumour cells in lymph nodes and the total number of lymph nodes that are affected
- Lymphovascular
- Perineural invasion
- CRCs with high-grade and its subtypes like poorly differentiated, undifferentiated carcinomas & signet ring cell variants
- Malignancy grade in the differentiation of carcinomas
- Expansile pattern of infiltration into the stroma
- Fibrosis due to desmoplastic changes in the stroma
- Involvement of the tumor with more of neuroendocrine cells
- Elevated levels of carcinoembryonic protein postoperatively within one year of tumor resection

- Lymphocyte infiltration into a tumour has been shown to be a significant prognostic indicator in a number of studies
- Presentation with perforation or obstruction
- Presence of genetic aberration in BRAF, RAS genes and mismatch repair deficiency

Factors associated with good prognosis

- Neoadjuvant chemoradiotherapy is associated with considerable tumour response and downstaging in suitably chosen patients with rectal cancer[41]
- Increased number of CD4+ and CD25+ T cells
- Presence of tumor beyond the splenic flexure

SYNDECAN 1(CD 138)

There is widespread expression of the transmembrane proteoglycan syndecan-1 (CD138) in both normal and malignant tissues.[6]

Syndecan-1 is encoded by the chromosome 2 gene SDC1.[44]

The core protein of syndecan-1 has two intracellular and extracellular domains. Heparan sulphate and chondroitin sulphate glycosaminoglycans are used in place of the extracellular domain. It is possible to reduce the adhesion between cell-to-cell and cell-to-basement membrane adhesions that are present in the stroma of various tumours by cleaving a portion of this Syndecan-1 at the junction between the cell membrane and extracellular site. This can aid in tumour progression by suppressing, transforming, and migrating.[7,45]

Reduced Syndecan-1 expression is related with tumour differentiation, progression, and clinical staging in colorectal cancers.[7] Syndecan-1, E-cadherin, and beta-catenin complex expression are typically disrupted in CRCs.[8]

To evaluate syndecan-1, Western blot, ELISA, and immunohistochemistry techniques are utilized. Evaluation of Syndecan-1 is crucial as a predictive tool because of its significance and role as a target for Indatuximab, a monoclonal antibody combined with a cytotoxic agent, due to its differential expression in tumours.[6]

Together, integrins and FAK are activated more quickly when Sdc-1 is reduced, and this results in signals that promote cancer stem cell characteristics and invasiveness. [46]

Syndecan-1 regulates the molecular mediators of tumour cell survival, proliferation, angiogenesis, and metastasis and is seen expressed by the surface of epithelial cells in mature tissues.[8]

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY DESIGN: Laboratory based observational Study

SOURCE OF DATA: The Department of Pathology at Sri Devaraj Urs Medical College, Tamaka, Kolar, received surgically resected colorectal cancer specimens from R.L. Jalappa Hospital and Research Center from October 2019 to November 2022. Additionally, the department also retrieved data and paraffin blocks for all colorectal cancer cases from the department's archives for the years 2008 to 2022.

DURATION OF STUDY: Two years

METHOD OF COLLECTION OF DATA: The Department of Pathology's archives were used to gather all Colorectal Cancer cases from 2008 to 2022, along with clinical information.

INCLUSION CRITERIA: All cases with histological diagnosis of colorectal carcinoma were admitted and underwent surgical resection in RLJH from 2008 to 2022.

EXCLUSION CRITERIA:

- Patients subjected to neoadjuvant radiotherapy/chemotherapy before excision of colorectal carcinoma.
- Patients who underwent chemotherapy for other cancers over the past five years.

SAMPLE SIZE: 91

Based on Antigony Mitselou et al.[8] survey of Syndecan-1 expression in colorectal carcinomas (62.32%) with 95% confidence intervals and a 10% absolute error, the sample size for the current investigation has been estimated at 91.

Formula for calculating sample size

Sample size is equal to $\frac{Z1\text{-}p(1\text{-}p)}{d2.}$

Z 1- = Standard normal variation in this case.

P = Population Expected Proportion based on Prior Studies

10% absolute inaccuracy is given by d.

In the current investigation, 91 colorectal cancer patients were included using the aforementioned values at a 95% Confidence Interval.

METHODOLOGY

All the clinicopathological data of colorectal carcinoma cases, such as age, sex, histological grading, lymph node status, and staging, were collected. The resected specimens of all colorectal carcinoma, confirmed histopathologically, were included in the study. H & E To perform immunohistochemistry against Syndecan-1 (rabbit monoclonal antibody, prediluted, Biogenex) for all cases of colorectal cancer, slides from all cases were evaluated, tumour tissue was chosen, and the peroxidase and anti-peroxidase method was used. Positive and negative controls were carried out on each patient.

IMMUNOHISTOCHEMISTRY PROTOCOL:

- Sections are cut at 3-4 μm, floated on positively charged slides, incubated at 37 degrees 1 day, and further at 58 degrees overnight.
- Do not allow it to dry at any stage.
- Carry out steps of incubation with the antibody at 37 degrees.
- Deparaffinization carried out in 15-minute intervals with xylene-I and xylene-II.
- Dexylinisation with Absolute Alcohol I and II administered for a minute each
- Dealcoholisation for 1 minute
- Distilled water five min-Washing
- Antigen Retrieval using the microwave at power 10 for 6 minutes in citrate buffer pH 6.0
- Transfer to TBS buffer pH (7.6)-15 minutes three times, washing for 5 minutes
- Preparation of peroxidase block for 30 minutes.

- Power Block will be done for 10 minutes.
- Drain and cover section with Primary Antibody
- Wash with TBS buffer for 5 minutes three times to wash unbound antibodies
- Secondary Antibody for 30 minutes
- Super enhancer
- TBS buffer wash 5 min three times
- Colour development with a working color development solution for 5-8 minutes
- Distilled water wash for 5 minutes.
- Counterstain with Harris hematoxylin for one minute
- Dehydration
- Mount with DPX

POSITIVE CONTROL: Tonsil was taken as a positive control.

EVALUATION OF SYNDECAN-1 IMMUNOSTAINING[47]

Syndecan-1 membranous/cytoplasmic staining was graded on a scale of 0 to 3, with 0 denoting no staining, 1 denoting faint staining, 2 denoting moderate staining, and 3 denoting high staining.

The following formula was used to determine the percentage of positively stained cells: (0, no stain; 1, 1-25%; 2, 26-50%; 3, > 50%).

A final score of 1-6 was obtained by combining the intensity and percentage scores.

A low-expression group (scores 0-2) and a high-expression group are created from the total score (scores 3-6).

STATISTICAL ANALYSIS:

The study's data were input into a Microsoft Excel data sheet and analyzed using SPSS 22 software. In order to depict the current variable and its values, Data was analyzed using frequency and proportional analysis. To determine if there was a statistically significant relationship between two sets of qualitative data, the chi-square test or Fischer's exact test (only for 2x2 tables) was used. Continuous data were used to illustrate the mean and standard deviation.

Data visualization: Several types of graphs were produced using Microsoft Word and Excel.

After considering all of the guidelines for statistical tests, a p-value (Probability that the result is accurate) of 0.05 was deemed to be statistically significant.

Statistical software utilized for analysis: MS Excel and IBM SPSS Statistics, Somers, NY, USA.

OBSERVATION AND RESULTS

RESULTS

Age distribution of subjects (n=95)

	Frequency	Percent
20-29yrs	3	3.2
30-39yrs	5	5.3
40-49yrs	15	15.8
50-59yrs	20	21.1
60-69yrs	33	34.7
70-79yrs	15	15.8
80-89yrs	4	4.2
Total	95	100.0

Table 4: Categorical subjects distribution by to age.

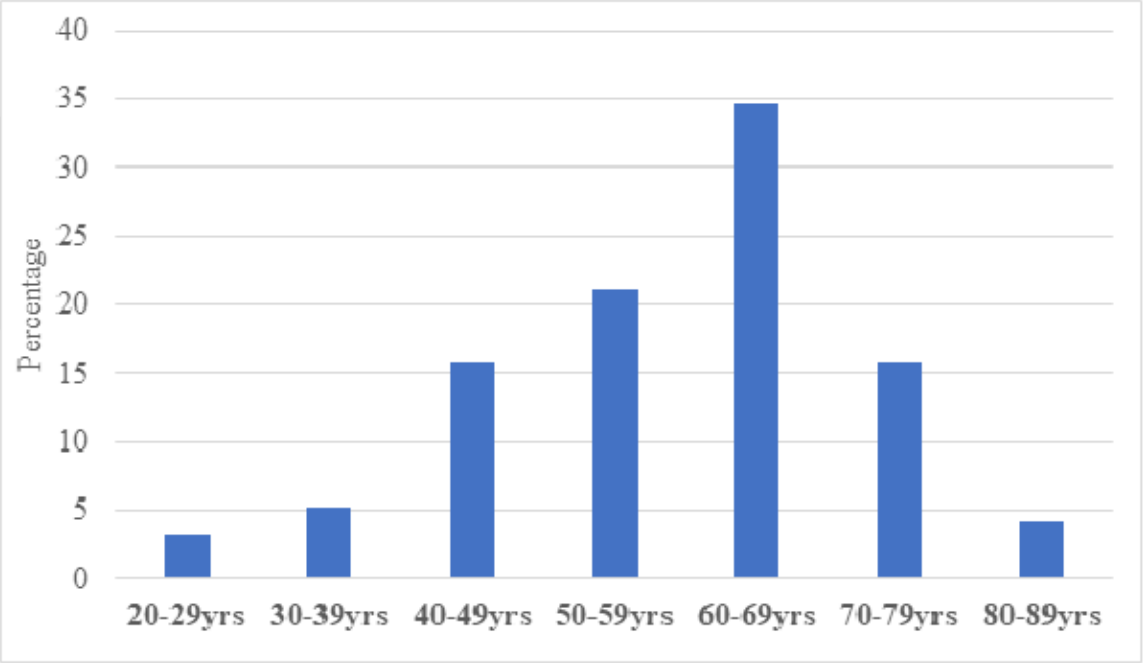


Chart 1: Categorical subjects distribution by to age.

Gender distribution of subjects (n=95):

	Frequency	Percent
Female	42	44.2
Male	53	55.8
Total	95	100.0

Table 5: Categorical subjects distribution by sex

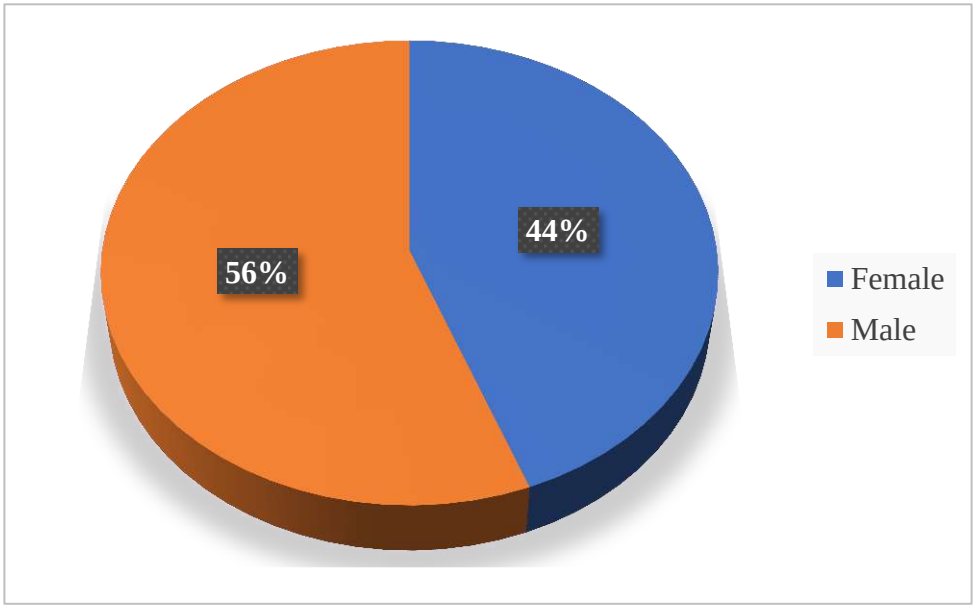


Chart 2: Categorical subjects distribution by sex

Categorical subjects distribution by site of tumor (n=95):

	Frequency	Percent
Ascending colon	21	22.1
Descending colon	11	11.6
Rectum	41	43.2
Sigmoid colon	15	15.8
Transverse colon	7	7.4
Total	95	100.0

Table 6: Categorical subjects distribution by site of tumor

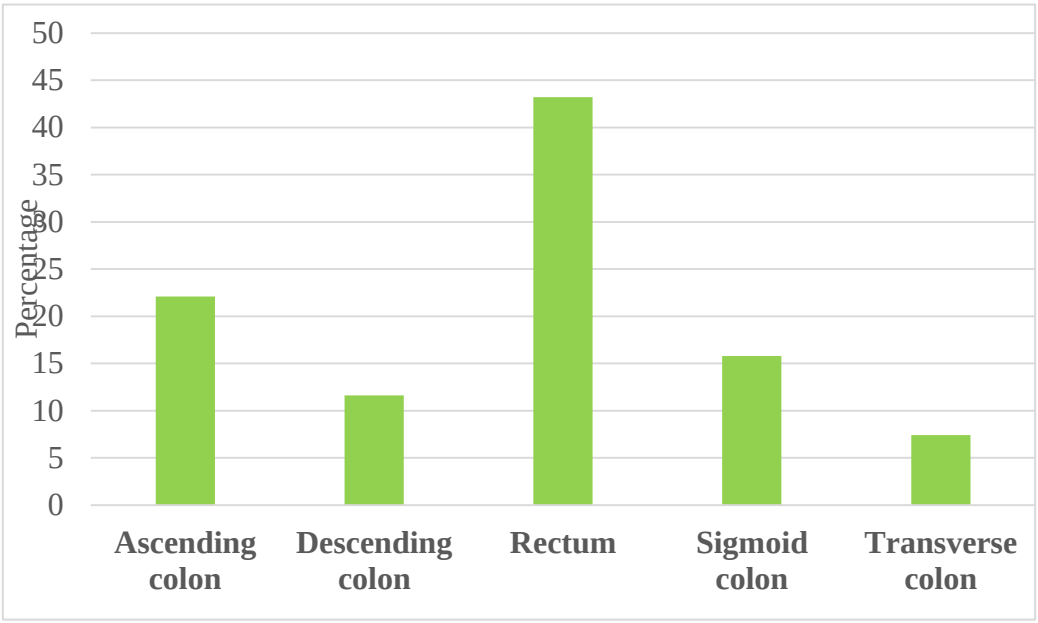


Chart 3: Categorical subjects distribution by site of tumor

Distribution of subjects according to malignancy grading (n=95):

	Frequency	Percent
Well-differentiated	36	37.9
Moderately differentiated	40	42.1
Poorly differentiated	19	20.0

Table 7: Distribution of subjects according to malignancy grading

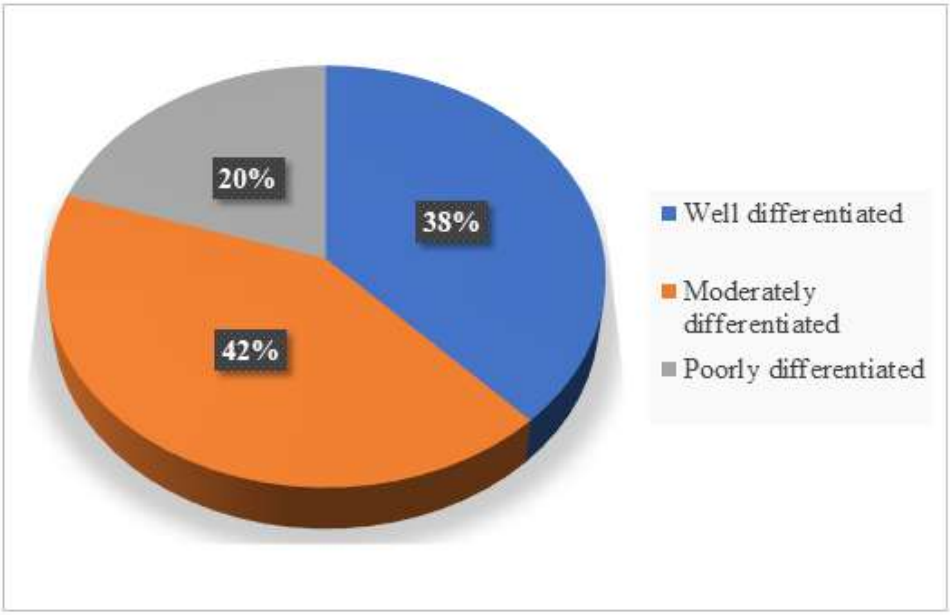


Chart 4: Distribution of subjects according to malignancy grading

Categorical subjects distribution by stage of the tumor (n=95):

	Frequency	Percentage
Stage I	25	26.31
Stage II	29	30.52
Stage III	41	43.15

Table 8: Categorical subjects distribution by stage of the tumor

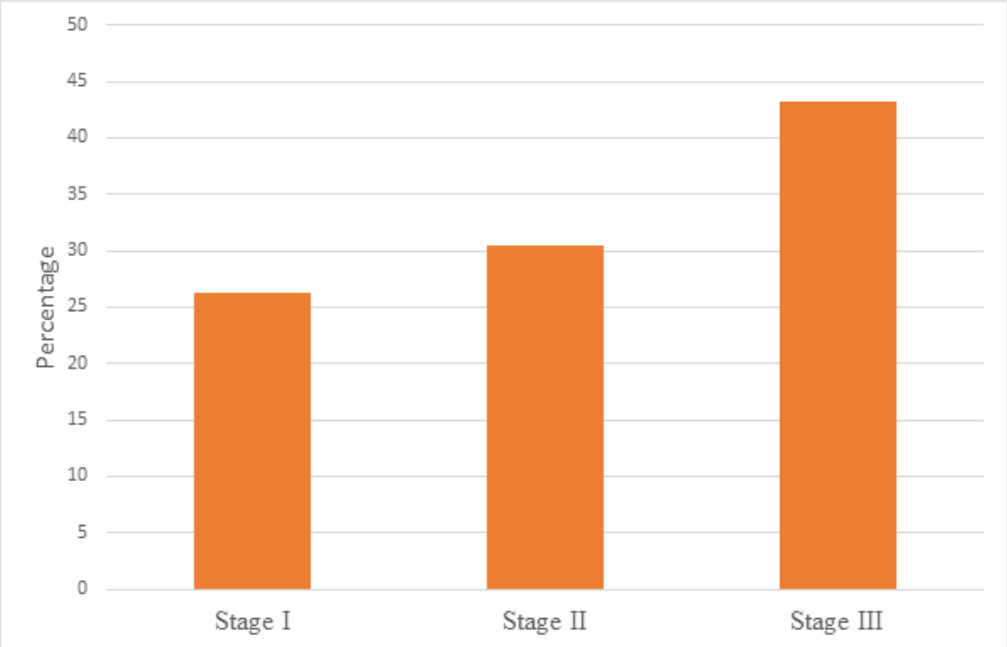


Chart 5: Categorical subjects distribution by stage of the tumor

Categorical subjects distribution by tumor size (n=95):

	Frequency	Percentage
T1	4	4.21
T2	26	27.36
T3	53	55.78
T4	12	12.63

Table 9: Categorical subjects distribution by tumor size

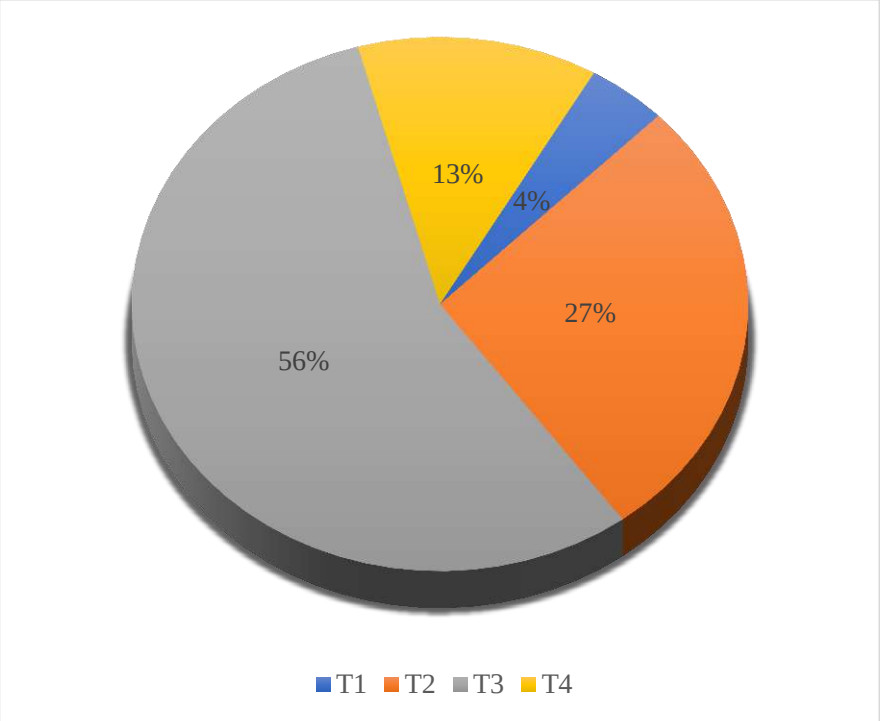


Chart 6: Categorical subjects distribution by tumor size

Categorical subjects distribution lymph node status (n=95):

	Frequency	Percent
Negative	55	57.9
Positive	40	42.1
Total	95	100.0

Table 10: Categorical subjects distribution lymph node status

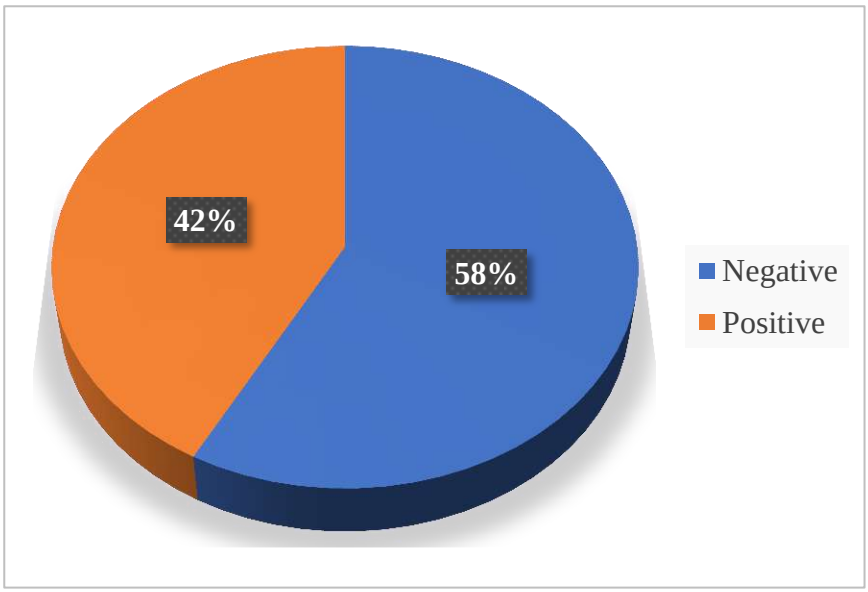


Chart 7: Categorical subjects distribution lymph node status

Distribution of subjects according to Vascular Invasion (n=95):

	Frequency	Percent
Absent	87	91.6
Present	8	8.4
Total	95	100.0

Table 11: Distribution of subjects according to Vascular Invasion

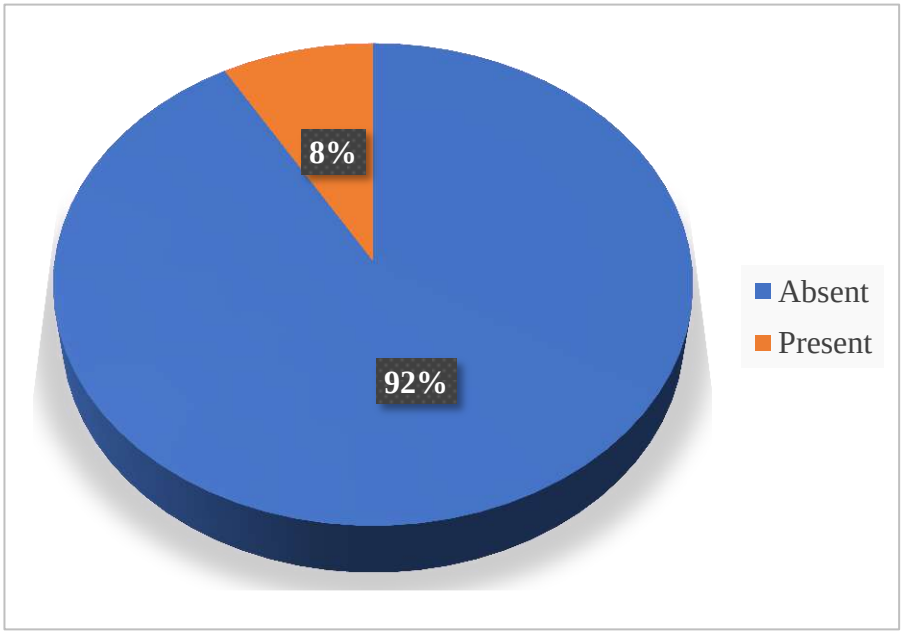


Chart 8: Distribution of subjects according to Vascular Invasion

Distribution of subjects according to Perineural invasion (n=95):

	Frequency	Percent
Absent	93	97.9
Present	2	2.1
Total	95	100.0

Table 12: Distribution of subjects according to Perineural invasion

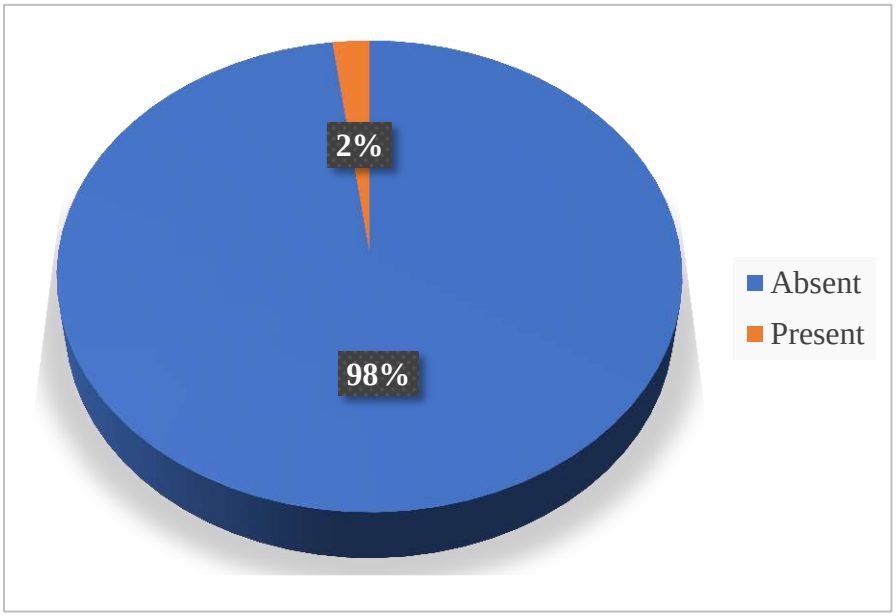


Chart 9: Distribution of subjects according to Perineural invasion

Categorical subjects distribution by Syndecan-1 expression (n=95):

	Frequency	Percent
HIGH	67	70.5
LOW	28	29.5
Total	95	100.0

Table 13: Categorical subjects distribution by Syndecan-1 expression

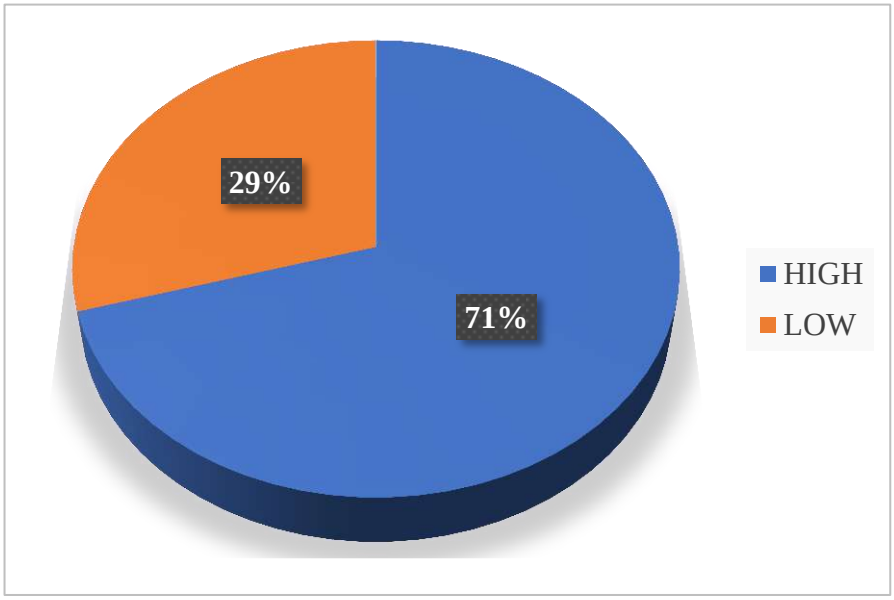


Chart 10: Categorical subjects distribution by Syndecan-1 expression

Distribution of subjects according to age group and expression

	High expression		Low expression	
	N	%	N	%
20-29yrs	1	33.3%	2	66.7%
30-39yrs	4	80.0%	1	20.0%
40-49yrs	10	66.7%	5	33.3%
50-59yrs	15	75.0%	5	25.0%
60-69yrs	24	72.7%	9	27.3%
70-79yrs	11	73.3%	4	26.7%
80-89yrs	2	50.0%	2	50.0%

Table 14: Distribution of subjects according to age group and expression

p-value 0.750, There was no discernible gap between high and low expression in this age bracket.

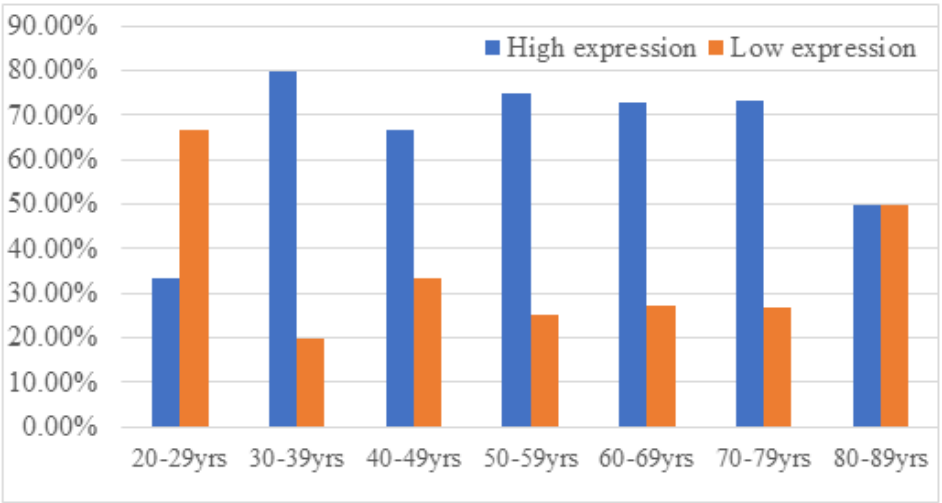


Chart 11: - Categorical subjects distribution by age group and Syndecan-1 expression.

Categorical subjects distribution by sex and Syndecan-1 expression

	High expression		Low expression	
	N	%	N	%
Female	34	81.0%	8	19.0%
Male	33	62.3%	20	37.7%

Table 15: Categorical subjects distribution by sex and Syndecan-1 expression

p-value 0.069, statistically significant difference was not found between high and low expression for sex.

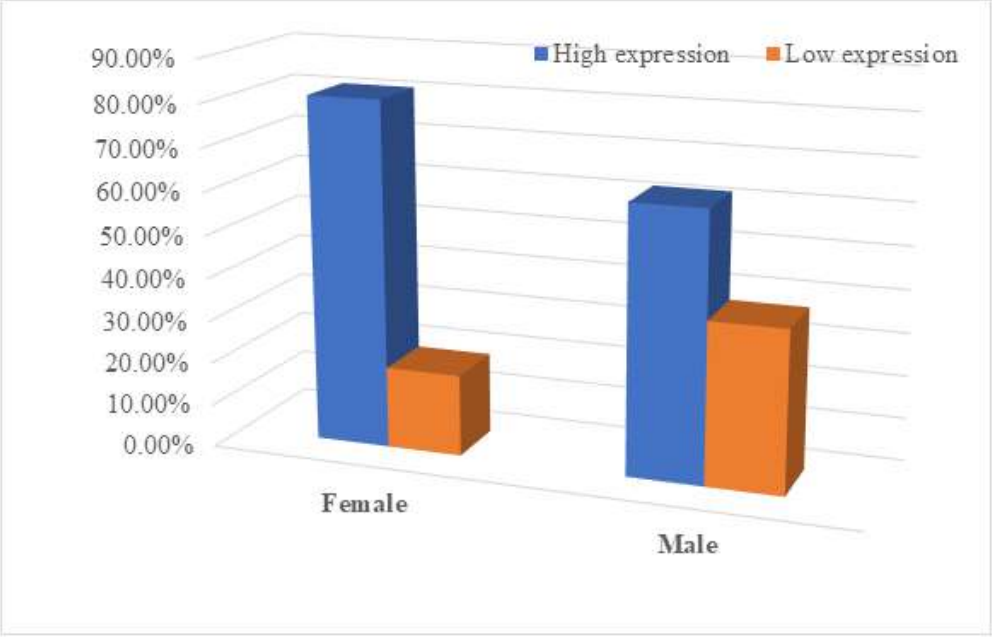


Chart 12: Categorical subjects distribution by sex and Syndecan-1 expression

Categorical subjects distribution by site and Syndecan-1 expression

	High expression		Low expression	
	N	%	N	%
Ascending colon	15	71.4%	6	28.6%
Descending colon	8	72.7%	3	27.3%
Rectum	27	65.9%	14	34.1%
Sigmoid colon	10	66.7%	5	33.3%
Transverse colon	7	100.0%	0	.0%

Table 16: Categorical subjects distribution by site and Syndecan-1 expression

p-value 0.478, no statistically significant difference was found between high and low expression for the site.

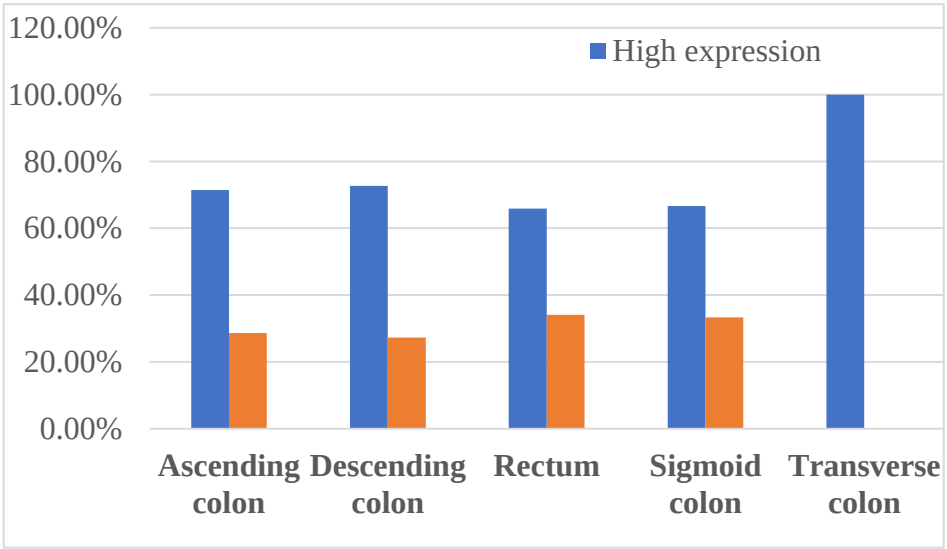


Chart 13: Categorical subjects distribution by site and Syndecan-1 expression

Categorical subjects distribution by malignancy grading and Syndecan-1 expression:

	High expression		Low expression	
	N	%	N	%
Well-differentiated	35	97.2%	1	2.8%
Moderately differentiated	30	75.0%	10	25.0%
Poorly differentiated	2	10.5%	17	89.5%

Table 17: Categorical subjects distribution by malignancy grading and Syndecan-1 expression

There was a statistically significant distinction between high and low expression with respect to malignancy grading was statistically significant ($p < 0.001$)

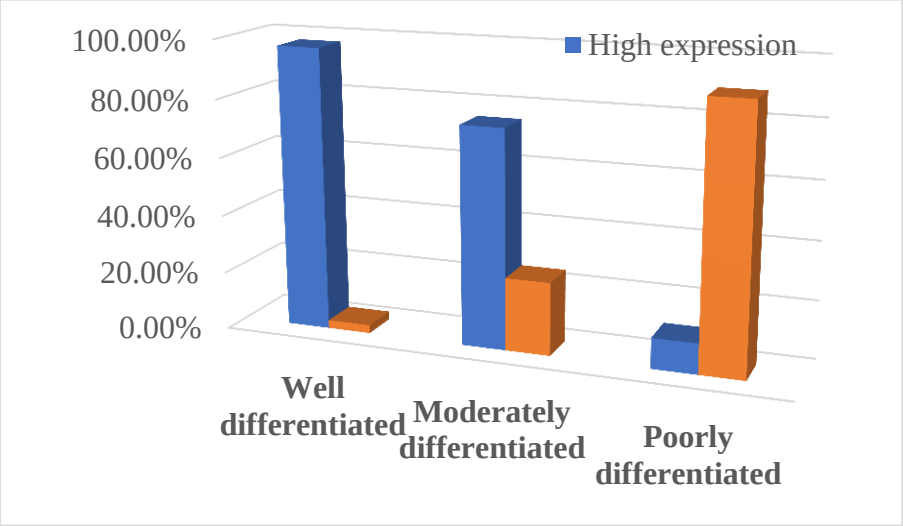


Chart 14: Categorical subjects distribution by malignancy grading and Syndecan-1 expression

Distribution of subjects according to staging and expression:

	High expression		Low expression	
	N	%	N	%
I	20	80.0%	5	20.0%
II	18	62.1%	11	37.9%
III	29	70.7%	12	29.3%

Table 18: Distribution of subjects according to staging and expression

p-value 0.354, no statistically significant difference between high and low expression for staging was found.

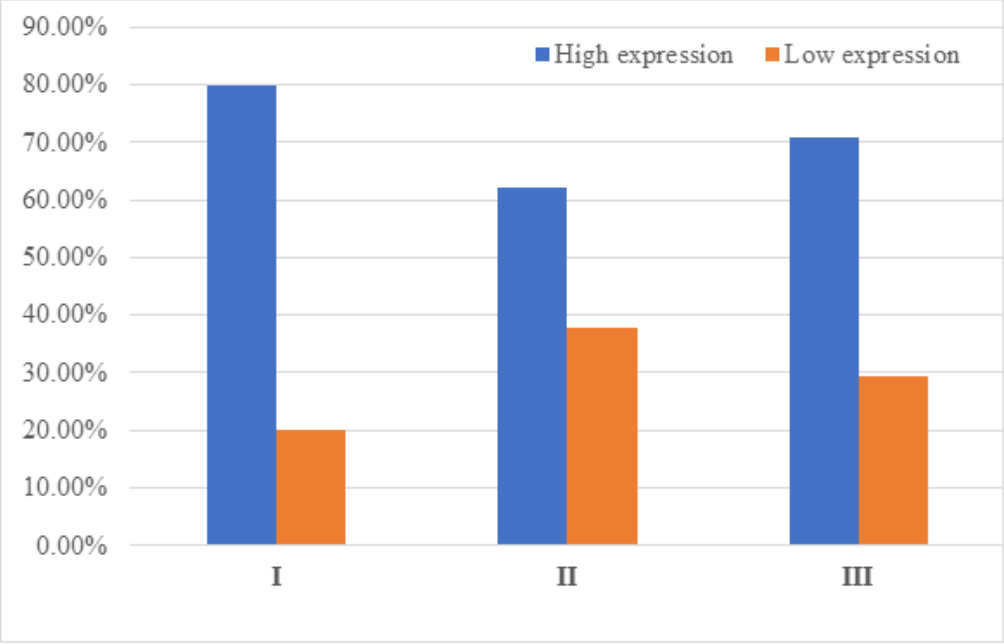


Chart 15: Distribution of subjects according to staging and expression

Categorical subjects distribution by tumor size and Syndecan-1 expression:

	High expression		Low expression	
	N	%	N	%
T1	3	75.0%	1	25.0%
T2	20	76.9%	6	23.1%
T3	39	73.6%	14	26.4%
T4	5	41.7%	7	58.3%

Table 19: Categorical subjects distribution by tumor size and Syndecan-1 expression

p-value 0.133, There was no discernible correlation between expression levels and tumour growth.

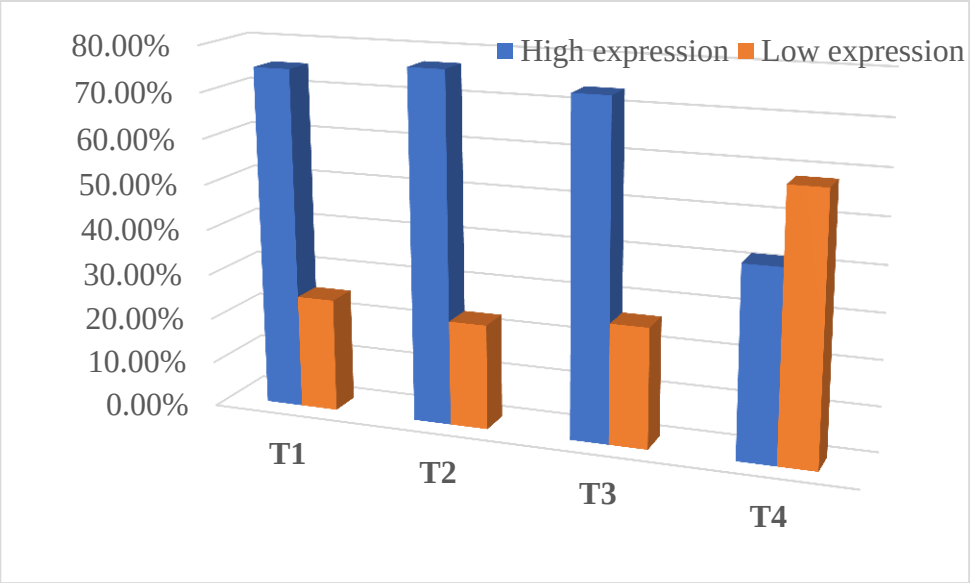


Chart 16: Categorical subjects distribution by tumor size and Syndecan-1 expression

Categorical subjects distribution by lymph node status and Syndecan-1 expression:

	High expression		Low expression	
	N	%	N	%
Negative	39	70.9%	16	29.1%
Positive	28	70.0%	12	30.0%

Table 20: Categorical subjects distribution by lymph node status and Syndecan-1 expression

p-value 1.00, no statistically significant difference between high and low expression for the lymph node was found.

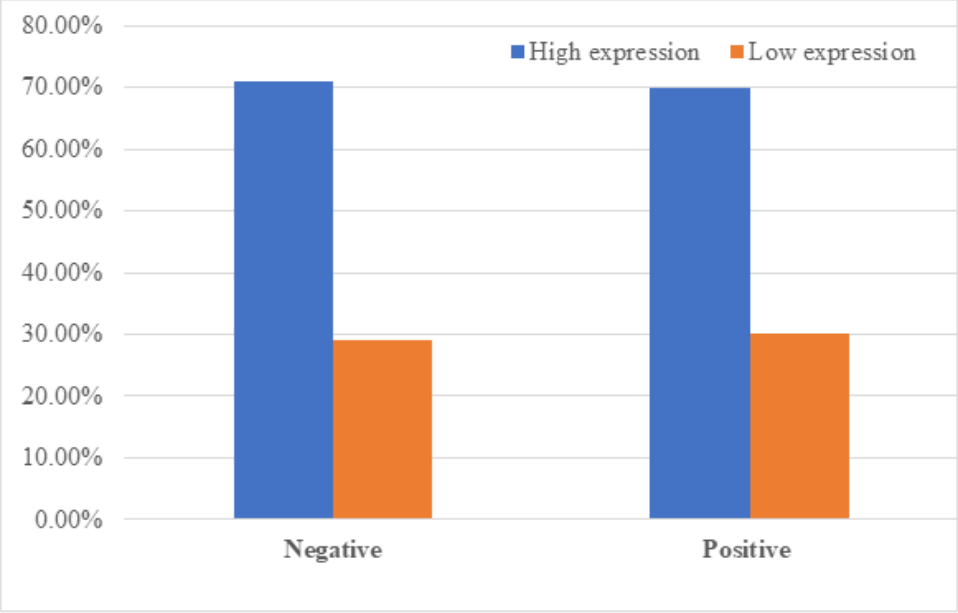


Chart 17: Categorical subjects distribution by lymph node status and Syndecan-1 expression

Categorical subjects distribution by Vascular Invasion and Syndecan-1 expression:

	High expression		Low expression	
	N	%	N	%
ABSENT	60	69.0%	27	31.0%
PRESENT	7	87.5%	1	12.5%

Table 21: Categorical subjects distribution by Vascular Invasion and Syndecan-1 expression

p-value 0.429 showed no statistically significant difference between high and low expression for vascular invasion.

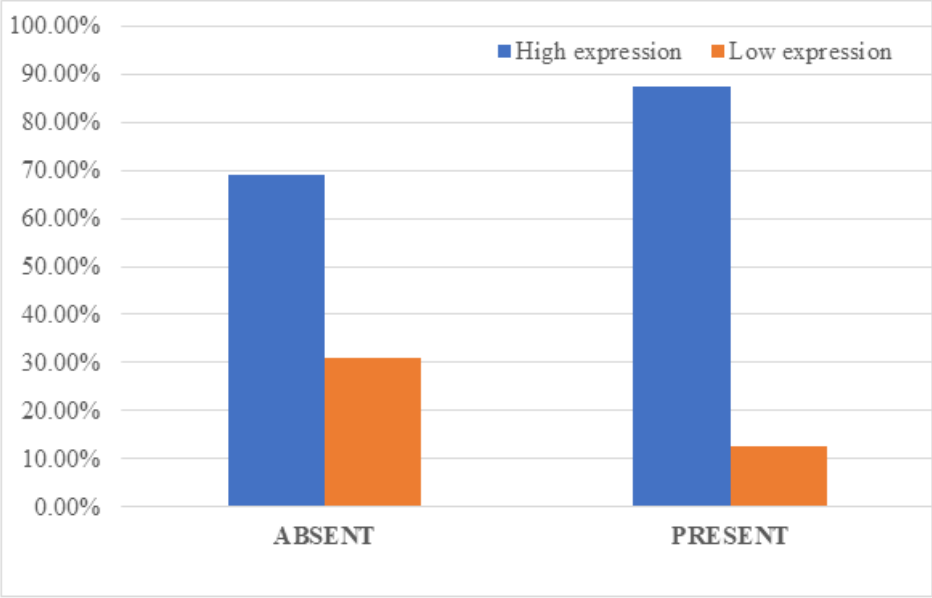


Chart 18: Categorical subjects distribution by Vascular Invasion and Syndecan-1 expression

Categorical subjects distribution by Perineural Invasion and Syndecan-1 expression:

	High expression		Low expression	
	N	%	N	%
ABSENT	66	71.0%	27	29.0%
PRESENT	1	50.0%	1	50.0%

Table 22: Categorical subjects distribution by Perineural Invasion and Syndecan-1 expression

p-value 0.505, no statistically significant difference between high and low expression for Perineural invasion was found.

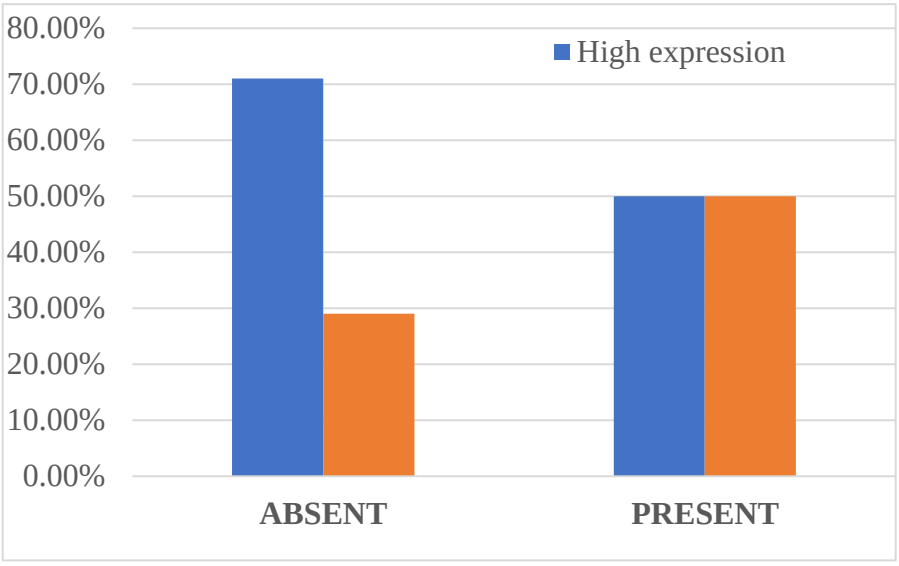


Chart 19: Categorical subjects distribution by Perineural Invasion and Syndecan-1 expression

Figure 5. Image showing proliferative growth in descending colon on cut section

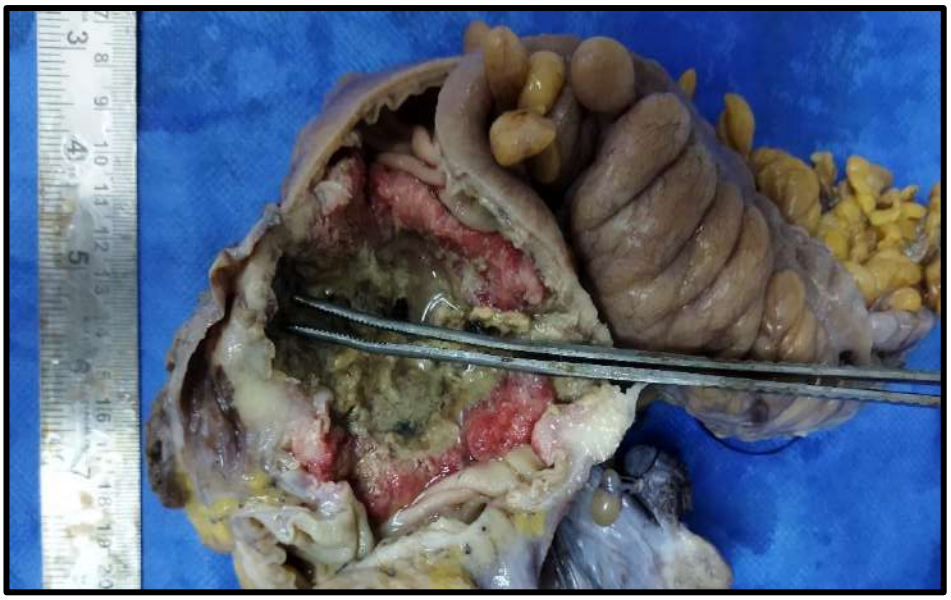


Figure 6. Image of ulcero-proliferative growth with central necrosis and involving the serosa in sigmoid colon

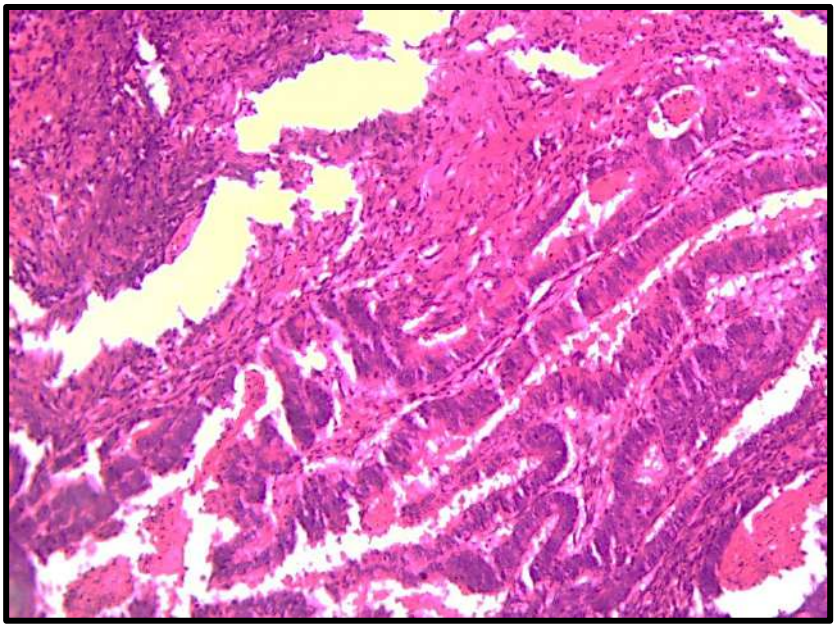


Figure 7: Microphotograph of H and E-stained section with 100x power showing Well Differentiated Adenocarcinoma

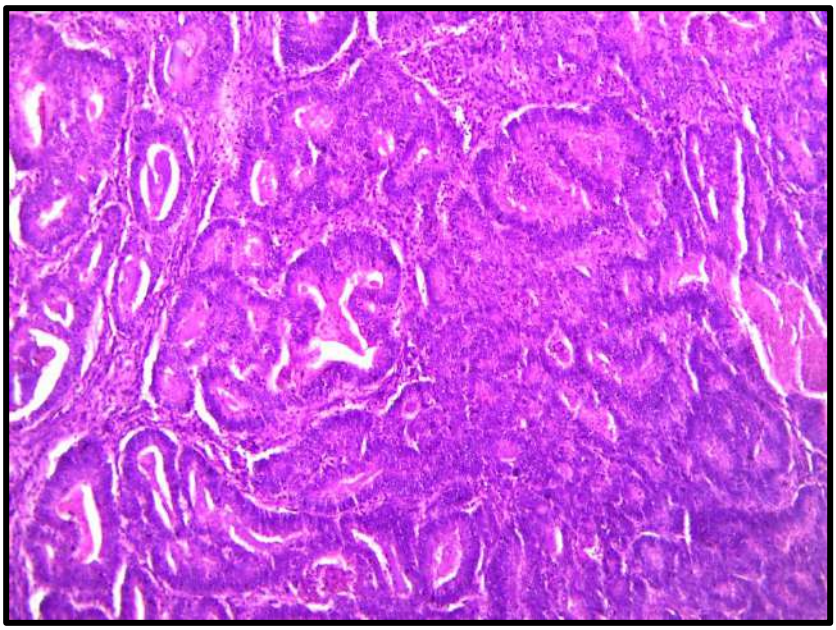


Figure 8: Microphotograph of H and E-stained section with 100x power showing Well Differentiated Adenocarcinoma

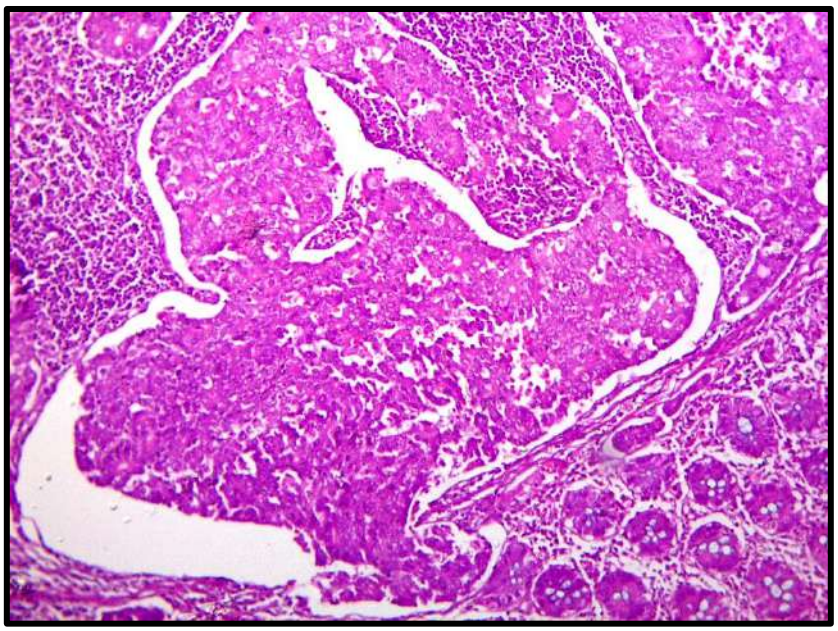


Figure 9: Microphotograph of H and E-stained section with 100x power showing Well Differentiated Adenocarcinoma

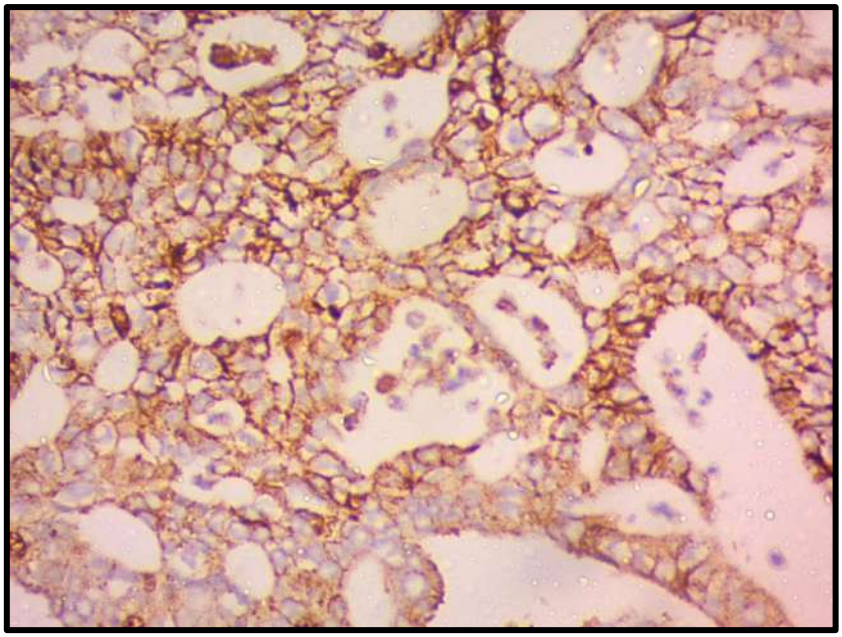


Figure 10. Microphotograph of Syndecan-1 IHC staining in 400X showing High expression in well differentiated colorectal carcinoma.

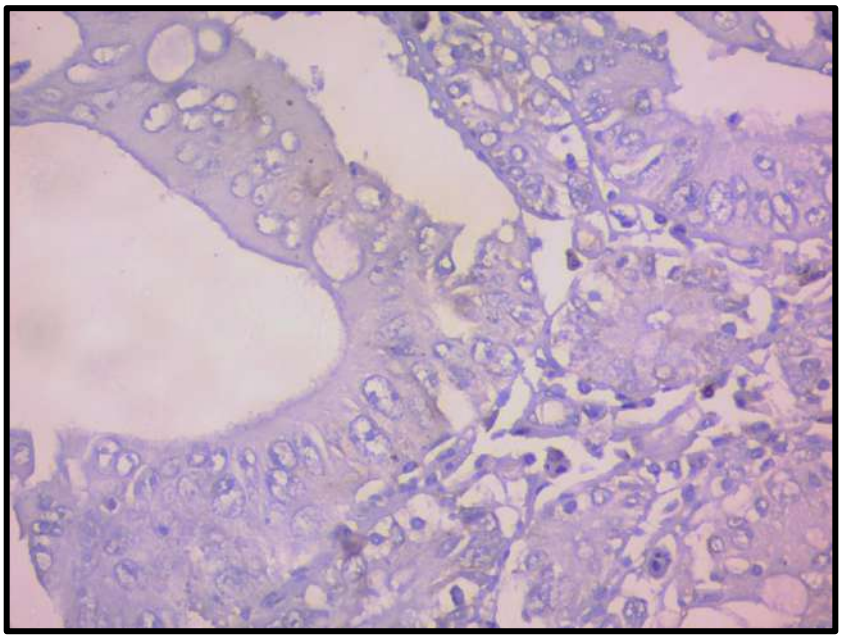


Figure 11. Microphotograph of Syndecan-1 IHC staining in 400X showing Low expression in poorly differentiated colorectal carcinoma.

DISCUSSION

DISCUSSION

CRCs are among the most frequently diagnosed cancers among men and women globally, according to the World Health Organization.[48]

Australia and New Zealand have a high incidence of colorectal cancer, but Africa and south-central Asia have a lower incidence.[49]

Age is one of the significant risk factors for the development of colorectal cancer. It is uncommon in people with age less than 40 years, and incidence increases with each succussing decade.[50]

Other factors that influence the outcome of colorectal carcinoma are sporadic CRCs or adenomatous polyps, inflammatory bowel disease, abdominopelvic radiation, cystic fibrosis, and hereditary CRC syndromes such adenomatous polyposis syndromes and Lynch syndrome.[24]

In addition to these factors CRC development is influenced by the use of red meat and the processed meat, use of tobacco in form of smoking or chewing, consumption of alcohol, and use of androgen deprivation therapy.[49]

Eight prognostic factors are now judged to be clinically significant in colorectal carcinoma, and they are as follows, Serum CEA levels, tumor regression score, circumferential resection margin from the edge of tumor to nearest dissected margins, lymphovascular invasion, perineural invasion, microsatellite instability, KRAS, and NRAS mutation and BRAF mutation.[4]

With cellular interactions and also as adhesion molecule between cell and the matrix. In malignant transformation epithelial expression of Syndecan-1 is lost which is more evident in poorly differentiated CRCs. Syndecan-1 is also a target of therapy for

Indatuximab. So, in all cases of colorectal cancer, epithelial Syndecan-1 expression.

Comparison of Age Distribution with other studies:

Study	Age
Al-Maghrabi J. et al. (2021) (n=202)	<60 years 108
	>60 years 94
Li K et al. (2017) (n=477)	<60.5 years 211
	>60.5 years 266
Mitselou et al (2022) (n=69)	40-81 years
The present study (n=95)	<60 years 54
	>60 years 41

Table 23: Comparison of Age Distribution with other studies

In this study, out of 95 cases, 54 (56.84%) were in the age group ≤ 60 years, and 41 (43.15%)were in the age group >60 years.

Peak incidence was in the 60-69 age group (34.7%).

In other studies, such as Al-Maghrabi et al.[47] (n=202) ≤ 60 years were 108 and > 60 years were 94 subjects, Li K et al.[51] (n=477) ≤60.5 years were 211 and > 60.5 years were 266 subjects, Mitselou et al.[8] (n=69) age range was around 40-81 years.

Comparison of Sex Distribution with other studies:

Study	Male %	Female %
Al-Maghrabi J. et al. (2021) (n=202)	55	45
Li K et al. (2017) (n=477)	48	52
Mitselou et al (2016) (n=69)	61	39
The present study (n=95)	56	44

Table 24: Comparison of Sex Distribution with other studies

Though there is no sex predilection for colorectal carcinoma, most studies show a higher prevalence of colorectal carcinoma in males. In the present study, males 55% and females 45% were seen. Compared with other studies like Al-Maghrabi et al.[47] Mitselou et al.[8] In a study by Li K et al.[51] Females were 52%, and males were 48%.

Comparison of location of tumor distribution with other studies:

Study	Site	
Al-Maghrabi J. et al. (2021) (n=202)	Right colon	25.7 %
	Left colon	62.9 %
	Rectum	11.4 %
Li K et al. (2019) (n=477)	Right colon	74 %
	Left colon	36 %
Theodoro T R et al (2022) (n=24)	Colon	37.5 %
	Rectum	62.5 %
The present study (n=95)	Ascending colon	22.1 %
	Descending colon	11.6 %
	Rectum	43.2 %
	Sigmoid colon	15.8 %
	Transverse colon	7.4 %

Table 24: Comparison of location of tumor distribution with other studies

In the present study, most of the cases were in the rectum (43.2%), followed by the sigmoid colon (15.8%), ascending colon (22.1%), descending colon (11.6%), and transverse colon (7.4%). Our study was similar to the survey done by Theodoro T R et al.[52] where most of the cases were in the rectum (62.5%) followed by the colon (37.5%), and also with the study done by Li K et al.[51] where colorectal carcinoma was primarily seen in right colon 74% than in left colon 36%.

Our study was contrary to the survey done by Al-Maghrabi et al.[47] where most of the cases seen in the left colon 62.9% followed by the right colon25.7% and the rectum being 11.4%.

Comparison of Tumor Size with other studies:

		Al-Maghrabi J. et al. (2021) (n=202)	Li K et al. (2017) (n=477)	Theodoro T R et al (2022) (n=24)	Present study (n=95)
Tumor size	<50 mm	45%	64%	58.3%	47.3%
	>50 mm	55%	36%	41.7%	54.7%

Table 25: Comparison of Tumor Size with other studies

The present study had a tumor size ≥50 mm in 54.7% of cases. The present study was similar to the survey done by AL-Maghrabi et al. (55%).[47] But our study was contrary to other studies by Ii K et al.[51] (36%) and Theodoro T R et al.[52] where they showed tumor size <50 mm being more cases.

Comparison of Histological Grading with other studies:

		Al-Maghrabi J. et al (2021) (n=202)	Li K et al. (2017) (n=477)	Mitselou et al (2016) (n=69)	Theodoro T R et al (2022) (n=24)	Present study (n=95)
Malignancy Grading	Well Differentiated	21.3%	47.3 %	4.35%	8.3%	37.9%
	Moderately Differentiated	65.8%	52.7%	85.51%	91.7%	42.1%
	Poorly Differentiated	12.9%		10.14%		20%

Table 26: Comparison of Histological Grading with other studies

In this study, most of the tumors 42.1% were graded as moderately differentiated, followed by 37.9 % of the well-differentiated tumor and 20% of the poorly differentiated tumor. This is similar to studies were done by Al-Maghrabi et al.[47] Li K et al.[51] Mitselou et al., and Theodoro T R et al.[52] where predominant tumors were graded as moderately differentiated.

Comparison of Pathological T Staging Distribution with other studies:

		Al-Maghrabi J. et al. (2021) (n=202)	Li K et al. (2017) (n=477)	Theodoro T R et al (2022) (n=24)	Present study (n=95)
T Staging	T1	12.9 %	14.46 % (T1 and T2)		4.21 %
	T2	1.5 %		25 %	27.36 %
	T3	15.8 %	85.53 % (T3 and T4)	75%	55.78 %
	T4	73.8 %			12.63 %

Table 27: Comparison of Pathological T Staging Distribution with other studies

The current study had more cases in T2 and T3 stages (68.41%), which was similar to studies done by Al-Maghrabi et al.[47] (89.6%) Li K et al.[51] (86.53%) and Theodoro T R et al.[52](75%)

Comparison of Pathological N Staging Distribution with other studies:

		Al-Maghrabi J. et al. (2021) (n=202)	Li K et al. (2017) (n=477)	heodoro T R et al (2022) (n=24)	Present study (n=95)
N Staging	N 0	54.9 %	60.79%	65.22 %	57.9 %
	N 1 and N 2	45.1 %	39.2 %	34.78 %	42.1 %

Table 28: Comparison of Pathological N Staging Distribution with other studies

In the present study, 57.9% of cases were in N0 Stage, followed by 42.1% in N1 and N2. This is similar to other studies such as Al-Maghrabi et al.[47], Li K et al.[51] and Theodoro T R et al.[52] where N0 stage was seen in 54.9 %, 60.79%, and 65.22%, respectively.

Comparison of Vascular Invasion with other studies:

		Al-Maghrabi J. Et al. (2021) (n=202)	Mitselou et al (2016) (n=69)	eodoro T R et al (2022) (n=24)	Present study (n=95)
Vascular Invasion	Absent	84.7 %	27.54 %	33.3 %	91.6 %
	Present	15.3 %	72.46 %	66.6 %	8.4 %

Table 29: Comparison of Vascular Invasion with other studies

Vascular invasion is an important prognostic factor in colorectal carcinoma. In the present study, only 8.4% of cases showed vascular invasion. The present study is similar to a study done by Al-Maghrabi et al.[47] which showed 15.3% of patients with vascular invasion. In contrast to other studies by Mitselou et al. 8 and Theodoro et al. 53, more vascular invasions were seen in 72.46% and 66.6% of cases.

Comparison of perineural Invasion with other studies:

		Theodoro T R et al (2022) (n=24)	The present study(n=95)
Perineural Invasion	Absent	79.2 %	97.9%
	Present	20.8 %	2.1%

Table 30: Comparison of perineural Invasion with other studies

Perineural is a critical prognostic factor in colorectal carcinoma. In the present study, only 2.1% of cases had a perineural invasion, similar to a study done by Theodoro et al.[52] which had 20.8% of patients with perineural invasion.

Comparison of expression of Syndecan-1 Scoring and Malignancy grading with other studies:

		High expression	Low expression
		%	%
The present study (n=95)	Well-differentiated	97.2%	2.8%
	Moderately differentiated	75.0%	25.0%
	Poorly differentiated	10.5%	89.5%
Al-Maghrabi J. Et al. (2021) (n=202)	Well-differentiated	70.7%	29.3%
	Moderately differentiated	63.9%	36.1%
	Poorly differentiated	57.1%	42.9%

Table 31: Comparison of expression of Syndecan-1 Scoring and Malignancy grading with other studies

In the current investigation, well-differentiated adenocarcinomas displayed high expression of Syndecan-1 immunohistochemistry, whereas poorly differentiated adenocarcinomas displayed low expression of Syndecan. The current study is in contrast to a study done by Al-Maghrabi et al.[47] where high expression was in both well-differentiated adenocarcinomas and poorly differentiated adenocarcinomas.

Parameter		High expression		Low expression		Test	p value
		N	%	N	%		
Age	20-29yrs	1	33.30%	2	66.70%	Chi-square test	0.75
	30-39yrs	4	80.00%	1	20.00%		
	40-49yrs	10	66.70%	5	33.30%		
	50-59yrs	15	75.00%	5	25.00%		
	60-69yrs	24	72.70%	9	27.30%		
	70-79yrs	11	73.30%	4	26.70%		
	80-89yrs	2	50.00%	2	50.00%		
Sex	Female	34	81.00%	8	19.00%	Chi-square test	0.069
	Male	33	62.30%	20	37.70%		
Site	Ascending colon	15	71.40%	6	28.60%	Chi-square test	0.478
	Descending colon	8	72.70%	3	27.30%		
	Rectum	27	65.90%	14	34.10%		
	Sigmoid colon	10	66.70%	5	33.30%		
	Transverse colon	7	100.00%	0	0.00%		
Malignancy grade	Well differentiated	35	97.20%	1	2.80%	Chi-square test	<0.001
	Moderately differentiated	30	75.00%	10	25.00%		
	Poorly differentiated	2	10.50%	17	89.50%		
Tumor size	T1	3	75.00%	1	25.00%	Chi-square test	0.133
	T2	20	76.90%	6	23.10%		
	T3	39	73.60%	14	26.40%		
	T4	5	41.70%	7	58.30%		
Stage of the tumor	I	20	80.00%	5	20.00%	Chi-square test	0.354
	II	18	62.10%	11	37.90%		
	III	29	70.70%	12	29.30%		
Lymph node status	Negative	39	70.90%	16	29.10%	Chi-square test	1
	Positive	28	70.00%	12	30.00%		
Vascular invasion	Absent	60	69.00%	27	31.00%	Chi-square test	0.429
	Present	7	87.50%	1	12.50%		
Perineural invasion	Absent	66	71.00%	27	29.00%	Chi-square test	0.505
	Present	1	50.00%	1	50.00%		

Table 32: Syndecan-1 expression and its relation to clinicopathological parameters.

The relationship between Syndecan-1 expression and clinicopathological parameters:

In the current investigation, there was a statistically significant link between high Syndecan-1 expression in well-differentiated adenocarcinomas and low Syndecan-1 expression in poorly differentiated adenocarcinomas (p 0.001). In contrast to the current study, Al-Maghrabi et al.[47] found no statistically significant relationship between Syndecan-1 expression and malignancy grade (p=0.503).

In contrast to Al-Maghrabi et al.[47]and Li K et al.[51] whose studies reported p 0.001 and p=1, respectively, respectively, our research revealed no statistically significant link between lymph node positivity and Syndecan-1 expression (p=1) and this could be because of low lymph node positivity in our study in comparison to other studies.

In contrast to the current study, where there was no statistical significance with the expression of Syndecan-1 and T stage of the tumour, Li K et al. had substantial statistical significance with the T stage of the tumour which had 85.53% of cases in T3 & T4 stage. Research has shown that SDC1 is coexpressed with EMT markers (E-cadherin and β-catenin) in CRCs and that this coexpression is regulated during epithelial-mesenchymal transition (EMT). The loss of SDC1 expression in carcinoma cells reduces cell adhesion to the extracellular matrix and enhances cell motility and invasion.[51]

Similar to studies by Al-Maghrabi et al. and Li K et al.[47,51] there was no statistically significant relationship between the patient's age, sex, tumour location, tumour stage, vascular invasion, and perineural invasion in our investigation.

CONCLUSION

CONCLUSION

High Syndecan-1 expression is shown in well-differentiated adenocarcinomas, while low expression is seen in poorly differentiated adenocarcinomas of the colon and rectum and indirectly shows the outcomes of clinical treatments. IHC analysis of Syndecan 1 can be used to regularly assess prognostic relevance, which would aid in clinical outcome, as loss of Syndecan-1 expression is related with loss of differentiation.

SUMMARY

SUMMARY

- The present study was undertaken in the Department of Pathology, Sri Devaraj Urs Medical College, Tamaka, Kolar over a period of two years from October 2020 to November 2022.
- A total of 95 cases of Colorectal carcinoma who underwent surgical resection were studied. H & E Slides of all cases were reviewed and performed immunohistochemistry against Syndecan-1. Expression of Syndecan-1 was evaluated and correlated with clinicopathological data of cases such as age, sex, histological grading, lymph node status and staging.
- Peak incidence was in the 60-69 years age group (34.7%). Most common site of the tumor was rectum (43.2%). Majority of cases were in Stage III(43.15%).
- Expression of Syndecan-1 by immunohistochemistry was scored as low-expression group (scores 0-2) and a high-expression group (scores 3-6) from the total score based on membranous/cytoplasmic staining & percentage of positively stained cells.
- 70.5 % of cases demonstrated High expression & 29.5% of cases had Low expression of Syndecan-1
- High expression of Syndecan-1 in Well differentiated carcinomas and Low expression of Syndecan-1 in poorly differentiated carcinomas was significantly correlated with malignancy grade of the colorectal carcinomas.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Couchman JR. Syndecan-1 (Cd138), carcinomas and emt. International Journal of Molecular Sciences; 22. Epub ahead of print 2 April 2021. DOI: 10.3390/ijms22084227.
2. Bopanna S, Ananthakrishnan AN, Kedia S, et al. Risk of colorectal cancer in Asian patients with ulcerative colitis: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2017; 2: 269–276.
3. Kumar V, Abbas AK, Aster JC. The Gastrointestinal Tract. In: Robbins & Cotran Pathologic Basis of Disease. Elsevier, Inc., 2021, pp. 753–822.
4. Amin MB, Edge SB, Greene FL, et al. American Joint Committee on Cancer (AJCC). AJCC Cancer Staging Manual, https://link.springer.com/book/9783319406176 (2017, accessed 25 November 2022).
5. Galandiuk S, Netz U, Morpurgo E, et al. Colon and Rectum. In: Townsend CM (ed) Sabiston Textbook of Surgery. Elsevier Inc, 2022, pp. 1320–1400.
6. Kind S, Merenkow C, Büscheck F, et al. Prevalence of Syndecan-1 (CD138) Expression in Different Kinds of Human Tumors and Normal Tissues. Dis Markers; 2019. Epub ahead of print 2019. DOI: 10.1155/2019/4928315.
7. Wei H tang, Guo E na, Dong B guo, et al. Prognostic and clinical significance of syndecan-1 in colorectal cancer: A meta-analysis. BMC Gastroenterol; 15. Epub ahead of print 30 October 2015. DOI: 10.1186/s12876-015-0383-2.
8. Mitselou A, Galani V, Skoufi U, et al. Syndecan-1, Epithelial-Mesenchymal Transition Markers (E-cadherin/β-catenin) and Neoangiogenesis-related Proteins (PCAM-1 and Endoglin) in Colorectal Cancer | Anticancer Research. ANTICANCER RESEARCH 2016; 2271–2280.
9. Bruce M, Carlson. Digestive and Respiratory Systems and Body Cavities. In: Human

Embryology and Developmental Biology. Elsevier, Inc, 2019, pp. 318–357.

10. Devi V S. Gastrointestinal Tract. In: Inderbir Singh's Human Embryology. New Delhi: Jaypee Brothers Medical Publishers, 2018, pp. 172–180.
11. Susan Standring. Large intestine . In: Gray's Anatomy. Elsevier Limited, 2021, pp. 1185–1204.
12. Krishna G. Small and Large Intestine. In: B D Chaurasia's Human Anatomy. New Delhi: CBS Publishers, 2018, pp. 291–300.
13. Pathology Outlines - Anatomy & histology, https://www.pathologyoutlines.com/topic/colonhistology.html (accessed 10 January 2023).
14. Bresalier R S. Colorectal Cancer. In: Sleisenger and Fordtran's Gastrointestinal and Liver Disease. Elsevier, Inc., 2021, pp. 2108–2152.
15. Gco.iarc. Cancer today, http://gco.iarc.fr/today/fact-sheets-cancers. (2021, accessed 28 November 2022).
16. Turnpenny P D, Ellard S, Cleaver R. The Genetics of Cancer…and Cancer Genetics . In: Emery's Elements of Medical Genetics and Genomics. Elsevier, Ltd., 2022, pp. 184–209.
17. Steele R J C. Colorectal cancer. In: Colorectal Surgery: A Companion to Specialist Surgical Practice. Elsevier Limited. , 2019, pp. 26–36.
18. Thompson MR, Heath I, Ellis BG, et al. Identifying and managing patients at low risk of bowel cancer in general practice. Br Med J 2003; 327: 263–265.
19. Goldblum J R. Large Bowel. In: Rosai and Ackerman's Surgical Pathology. Elsevier Inc., 2018, pp. 648–702.
20. Mangi FH, Shaikh TA, Soria D, et al. Novel molecular classification of colorectal cancer and correlation with survival. Saudi J Biol Sci 2022; 29: 3929–3936.
21. Edge, SB, Byrd, et al. AJCC (American Joint Committee on Cancer) Cancer Staging

Manual. 7th ed. New York: Springer, 2010.

22. Shepherd NA, Baxter KJ, Love SB. The prognostic importance of peritoneal involvement in colonic cancer: a prospective evaluation. Gastroenterology 1997; 112: 1096–1102.

23. Kornprat P, Pollheimer MJ, Lindtner RA, et al. Value of tumor size as a prognostic variable in colorectal cancer: a critical reappraisal. Am J Clin Oncol 2011; 34: 43–49.

24. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA Cancer J Clin 2018; 68: 250–281.

25. Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? Journal of Clinical Oncology 2008; 26: 303–312.

26. Gosens MJEM, Klaassen RA, Tan-Go I, et al. Circumferential margin involvement is the crucial prognostic factor after multimodality treatment in patients with locally advanced rectal carcinoma. Clin Cancer Res 2007; 13: 6617–6623.

27. CC C, LP F, LJ B, et al. Prognostic factors in colorectal cancer. College of American Pathologists Consensus Statement 1999. Arch Pathol Lab Med 2000; 124: 43–53.

28. Swanson RS, Compton CC, Stewart AK, et al. The prognosis of T3N0 colon cancer is dependent on the number of lymph nodes examined. Ann Surg Oncol 2003; 10: 65–71.

29. Chang GJ, Rodriguez-Bigas MA, Skibber JM, et al. Lymph node evaluation and survival after curative resection of colon cancer: Systematic review. J Natl Cancer Inst 2007; 99: 433–441.

30. Baxter NN, Kennedy EB, Bergsland E, et al. Adjuvant Therapy for Stage II Colon Cancer: ASCO Guideline Update. Journal of Clinical Oncology 2022; 40: 892–910.

31. Liebig C, Ayala G, Wilks J, et al. Perineural invasion is an independent predictor of outcome in colorectal cancer. Journal of Clinical Oncology 2009; 27: 5131–5137.

32. Hyngstrom JR, Hu CY, Xing Y, et al. Clinicopathology and outcomes for mucinous and

signet ring colorectal adenocarcinoma: analysis from the National Cancer Data Base. Ann Surg Oncol 2012; 19: 2814–2821.

33. Chapuis PH, Dent OF, Fisher R, et al. A multivariate analysis of clinical and pathological variables in prognosis after resection of large bowel cancer. Br J Surg 1985; 72: 698–702.

34. Morikawa T, Kuchiba A, Qian ZR, et al. Prognostic significance and molecular associations of tumor growth pattern in colorectal cancer. Ann Surg Oncol 2012; 19: 1944–1953.

35. Caporale A, Bonapasta SA, Scarpini M, et al. Quantitative investigation of desmoplasia as a prognostic indicator in colorectal cancer. J Invest Surg 2010; 23: 105–109.

36. Liu Y, Xu J, Jiao Y, et al. Neuroendocrine differentiation is a prognostic factor for stage II poorly differentiated colorectal cancer. Biomed Res Int; 2014. Epub ahead of print 2014. DOI: 10.1155/2014/789575.

37. Konishi T, Shimada Y, Hsu M, et al. Association of preoperative and postoperative serum carcinoembryonic antigen and colon cancer outcome. JAMA Oncol 2018; 4: 309–315.

38. Mlecnik B, Tosolini M, Kirilovsky A, et al. Histopathologic-based prognostic factors of colorectal cancers are associated with the state of the local immune reaction. J Clin Oncol 2011; 29: 610–618.

39. Ho YH, Siu SKK, Buttner P, et al. The effect of obstruction and perforation on colorectal cancer disease-free survival. World J Surg 2010; 34: 1091–1101.

40. Medline ® Abstract for Reference 47 of 'Pathology and prognostic determinants of colorectal cancer' - UpToDate, https://www.uptodate.com/contents/pathology-and-prognostic-determinants-of-colorectal-cancer/abstract/47 (accessed 28 November 2022).

41. Ruo L, Tickoo S, Klimstra DS, et al. Long-term prognostic significance of extent of rectal cancer response to preoperative radiation and chemotherapy. Ann Surg 2002; 236: 75–81.

42. Salama P, Phillips M, Grieu F, et al. Tumor-infiltrating FOXP3+ T regulatory cells show

strong prognostic significance in colorectal cancer. Journal of Clinical Oncology 2009; 27: 186–192.

43. Petrelli F, Tomasello G, Borgonovo K, et al. Prognostic survival associated with left-sided vs right-sided colon cancer a systematic review and meta-analysis. JAMA Oncol 2017; 3: 211–219.

44. Ala-Kapee M, Nevanlinna H, Mali M, et al. Localization of gene for human syndecan, an integral membrane proteoglycan and a matrix receptor, to chromosome 2. Somat Cell Mol Genet 1990; 16: 501–505.

45. Piperigkou Z, Mohr B, Karamanos N, et al. Shed proteoglycans in tumor stroma. Cell and Tissue Research 2016; 365: 643–655.

46. Kumar Katakam S, Tria V, Sim WC, et al. The heparan sulfate proteoglycan syndecan-1 regulates colon cancer stem cell function via a focal adhesion kinase—Wnt signaling axis. FEBS Journal 2021; 288: 486–506.

47. Al-Maghrabi J. Loss of expression of syndecan-1 is associated with tumor recurrence, metastatic potential, and poor survival in patients with colorectal carcinoma. Pak J Med Sci 2021; 37: 1–7.

48. Colorectal cancer: Epidemiology, risk factors, and protective factors, https://www-uptodate-com-sduaherlibrary.knimbus.com/contents/colorectal-cancer-epidemiology-risk-factors-and-protective-factors/print?search…1/62 (2022).

49. Fitzmaurice C, Allen C, Barber RM, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol 2017; 3: 524–548.

50. Meester RGS, Mannalithara A, Lansdorp-Vogelaar I, et al. Trends in Incidence and Stage at Diagnosis of Colorectal Cancer in Adults Aged 40 Through 49 Years, 1975-2015.

JAMA 2019; 321: 1933–1934.

51. Li K, Li L, Wu X, et al. Loss of SDC1 expression is associated with poor prognosis of colorectal cancer patients in northern China. Dis Markers; 2019. Epub ahead of print 2019. DOI: 10.1155/2019/3768708.

52. Theodoro TR, Serrano RL, Turke KC, et al. Alterations of the Extracellular Matrix in Colorectal Carcinoma. Genet Test Mol Biomarkers 2022; 26: 468–475.

ANNEXURES

ANNEXURE - I INFORMED CONSENT FORM

INFORMED CONSENT FORM

STUDY TITLE: The immunohistochemical expression of syndecan 1(CD 138) and its correlation with staging and grading of colorectal carcinoma.

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:

Place:

Name and signature / thumb impression Date:

Place:

(Witness/Parent/ Guardian/ Husband)

ANNEXURE –II

PATIENT INFORMATION SHEET

PATIENT INFORMATION SHEET:

STUDY TITLE: The immunohistochemical expression of syndecan 1(CD 138) and its correlation with staging and grading of colorectal carcinoma.

PLACE OF STUDY: Department of Pathology, Sri Devaraj Urs Medical College, Kolar.

The main aim of the study is to find the role of syndecan 1 in colorectal carcinoma. 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 which you 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 Sudarshan K

ANNEXURE III

STUDY PROFORMA

PATIENT PROFORMA

Name:	
Age:	Hospital Number:

Anonymised Sample No:

Chief complaint:

History of presenting illness:

Past history:

Personal history:

Local examination:

Histopathological diagnosis:

Gross:

Microscopy:

Stage of disease:

KEY TO MASTER CHART

S. No = SERIAL NUMBER

UNIQUE HOSPITAL IDENTIFICATION NUMBERYEAR=YEAR OF BIOPSY

BIOPSY No= BIOPSY NUMBER

AGE= AGE IN YEARS

SEX: M= MALE F= FEMALE

SPECIMEN TYPE: APR= ABDOMINOPERINEAL

RESECTIONTNM=TUMOUR NODE METASTASIS

STAGING LN=LYMPHNODE

LN + = LYMPH NODE POSITIVE

LVI= LYMPHOVASCULAR INVASION

PNI= PERINEURAL INVASION

TOTAL IHC SCORE = TOTAL IHC SCORE

S.NO	HOSPITAL NO	YEAR	BIOPSY NO	AGE	SEX	SPECIMEN TYPE	SITE	HISTOPATH OLOGY DIAGNOSIS	MALIGNANCY GRADING	GROWTH	TNM	STAGING	TUMOR SIZE	LN+	LVI	PNI	Total IHC score
1	438421	2008	1002	35	M	APR	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	3
2	432848	2008	796	31	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	6
3	413277	2008	406	48	M	APR	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T4N0MX	II	<50MM	0	ABSENT	ABSENT	0
4	458197	2008	1510	50	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T2N1MX	III	>50MM	2	ABSENT	ABSENT	3
5	354632	2008	1264	70	M	HEMICOLECTOMY	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T4N0MX	II	>50MM	0	ABSENT	ABSENT	0
6	453464	2008	1344	68	M	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	6
7	456410	2008	1373	75	M	HEMICOLECTOMY	TRANSVERSE COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3CNXMX	II	<50MM	0	ABSENT	ABSENT	6
8	459520	2008	1743	40	F	ANTERIOR RESECTION	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T1N0MX	I	<50MM	0	ABSENT	ABSENT	6
9	470873	2008	1789	20	M	HEMICOLECTOMY	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T1N0MX	I	>50MM	0	ABSENT	ABSENT	6
10	470610	2008	1792	45	M	HEMICOLECTOMY	TRANSVERSE COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T2NXMX	I	<50MM	0	ABSENT	ABSENT	5
11	486531	2009	1510	60	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T2NXMX	I	<50MM	0	ABSENT	ABSENT	6
12	501634	2010	1388	48	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T4N1MX	III	>50MM	1	ABSENT	ABSENT	6
13	525369	2010	1937	52	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T2NXMX	I	<50MM	0	ABSENT	ABSENT	6
14	579655	2010	1504	47	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	PROLIFERATIVE	T4N1MX	III	<50MM	2	ABSENT	ABSENT	5
15	690751	2011	782	25	F	APR	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3aBnxmx	II	>50MM	0	ABSENT	ABSENT	3
16	638644	2011	1736	65	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N1MX	III	>50MM	3	ABSENT	ABSENT	0
17	733193	2011	1804	28	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3NXMX	II	>50MM	0	ABSENT	ABSENT	0
18	743282	2011	1098	54	F	APR	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3aBnxmx	II	>50MM	0	ABSENT	ABSENT	5
19	789154	2011	1461	46	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N1MX	III	>50MM	2	ABSENT	ABSENT	3
20	791325	2011	1664	60	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T2N1MX	III	>50MM	2	ABSENT	ABSENT	6
21	733105	2011	1994	52	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N1MX	III	>50MM	2	ABSENT	ABSENT	6
22	762580	2012	8	65	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	>50MM	2	ABSENT	ABSENT	4
23	770859	2012	146	75	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N1MX	III	>50MM	2	ABSENT	ABSENT	5
24	816143	2012	1358	67	M	APR	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T1NXMX	I	<50MM	0	ABSENT	ABSENT	4
25	835745	2012	1866	51	F	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	>50MM	1	ABSENT	ABSENT	4
26	840354	2012	1814	36	M	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	6
27	837910	2012	1790	73	F	APR	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N1MX	III	>50MM	2	ABSENT	ABSENT	6
28	841155	2012	2213	85	F	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T4N1MX	III	>50MM	1	ABSENT	ABSENT	2
29	836409	2012	2480	45	F	APR	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	<50MM	2	ABSENT	ABSENT	4
30	843857	2012	286	63	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	6

31	867145	2012	2387	49	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	>50MM	1	PRESENT	ABSENT	5
32	853324	2012	2480	74	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	6
33	819643	2012	349	80	F	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	>50MM	1	ABSENT	ABSENT	4
34	883254	2012	1167	62	M	APR	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	PROLIFERATIVE	T2NXMX	I	<50MM	0	ABSENT	ABSENT	6
35	899146	2012	1501	64	M	APR	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	<50MM	2	ABSENT	ABSENT	6
36	882182	2013	298	55	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N1MX	III	>50MM	2	ABSENT	ABSENT	4
37	878863	2013	331	60	M	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	>50MM	1	ABSENT	ABSENT	0
38	883102	2013	427	67	M	APR	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	PROLIFERATIVE	T2NXMX	I	<50MM	0	ABSENT	ABSENT	5
39	879624	2013	443	46	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	5
40	903057	2013	851	60	M	APR	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N1MX	III	>50MM	1	ABSENT	ABSENT	3
41	958439	2013	2098	65	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N2MX	III	>50MM	4	ABSENT	ABSENT	0
42	940986	2013	1844	65	F	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	PROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	6
43	928495	2013	1652	65	F	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	5
44	854002	2013	1714	70	F	APR	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	5
45	981042	2014	223	60	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N1MX	III	>50MM	1	ABSENT	ABSENT	2
46	940314	2014	568	73	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	PROLIFERATIVE	T4aN1cMX	IIIB	<50MM	3	ABSENT	ABSENT	2
47	931225	2014	893	64	M	APR	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T1NXMX	I	<50MM	0	ABSENT	ABSENT	2
48	967345	2014	1305	56	F	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	4
49	32776	2014	1999	50	F	APR	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	5
50	155065	2015	1593	60	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	>50MM	1	PRESENT	ABSENT	4
51	195235	2015	783	46	M	HEMICOLECTOMY	DESCENDINGCOLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	>50MM	0	ABSENT	ABSENT	2
52	213689	2015	1439	54	M	APR	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	0
53	208706	2015	3187	70	M	HEMICOLECTOMY	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T4BNXMX	IIB	>50MM	0	ABSENT	ABSENT	0
54	254597	2016	1885	45	F	HEMICOLECTOMY	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N0MX	IIA	<50MM	0	ABSENT	ABSENT	0
55	289663	2016	2936	60	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	PROLIFERATIVE	T4aN1cMX	IIIB	<50MM	3	ABSENT	ABSENT	3
56	305665	2016	2067	58	F	HEMICOLECTOMY	DESCENDINGCOLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	>50MM	0	ABSENT	ABSENT	3
57	218304	2016	48	68	M	APR	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	5
58	304816	2016	2001	76	F	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	6
59	428218	2017	1207	45	M	APR	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N2MX	IIIC	<50MM	6	PRESENT	PRESENT	0
60	402489	2017	474	45	F	APR	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	<50MM	3	PRESENT	PRESENT	6
61	502643	2017	2504	84	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	2
62	541581	2018	382	63	F	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	IIA	<50MM	0	ABSENT	ABSENT	6
63	553372	2018	1515	30	M	APR	RECTUM	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	<50MM	2	ABSENT	ABSENT	4

64	548316	2018	613	70	M	ANTERIOR RESECTION	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	III	<50MM	0	ABSENT	ABSENT	5
65	550703	2018	782	56	M	ANTERIOR RESECTION	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	5
66	615361	2018	2030	57	F	HEMICOLECTOMY	DESCENDINGCOLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N0M0	II	<50MM	0	ABSENT	ABSENT	6
67	655446	2019	253	65	M	HEMICOLECTOMY	DESCENDINGCOLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1bMX	IIB	<50MM	3	ABSENT	ABSENT	5
68	728096	2019	1532	55	F	HEMICOLECTOMY	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2NXMX	I	<50MM	0	ABSENT	ABSENT	6
69	700297	2019	728	72	M	HEMICOLECTOMY	TRANSVERSE COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1MX	III	>50MM	2	ABSENT	ABSENT	4
70	683154	2019	1467	65	F	APR	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	5
71	841770	2020	707	60	F	HEMICOLECTOMY	DESCENDINGCOLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	5
72	844349	2020	838	75	F	HEMICOLECTOMY	RECTOSIGMOID	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N0MX	I	<50MM	0	ABSENT	ABSENT	6
73	84806	2020	991	40	F	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T2N0MX	I	>50MM	0	ABSENT	ABSENT	5
74	846813	2020	1265	45	F	HEMICOLECTOMY	RECTUM	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T2N0MX	I	<50MM	0	ABSENT	ABSENT	6
75	867528	2020	1466	62	F	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3N1AMX	III	>50MM	1	ABSENT	ABSENT	6
76	866322	2020	1530	65	F	HEMICOLECTOMY	TRANSVERSE COLON	ADENOCARCINOMA	WELL DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	IIA	>50MM	0	ABSENT	ABSENT	6
77	875828	2020	1732	65	M	HEMICOLECTOMY	ASCENDING COLON	ADENOCARCINOMA	POORLY DIFFERENTIATED	ULCEROPROLIFERATIVE	T4AN0MX	IIB	<50MM	0	ABSENT	ABSENT	2
78	843200	2020	1209	35	M	HEMICOLECTOMY	RECTUM	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCEROPROLIFERATIVE	T3N0MX	II	<50MM	0	ABSENT	ABSENT	6
79	891338	2021	172	68	M	HEMICOLECTOMY	SIGMOID COLON	ADENOCARCINOMA	MODERATELY DIFFERENTIATED	ULCERATIVE/INFILTRATIVE	T3NXMX	II	<50MM	0	ABSENT	ABSENT	6
80	903275	2021	578	65	M	Hemicolectomy	Rectosigmoid junction	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T3N2bMx	IIIC	>50mm	2	Absent	Absent	3
81	943507	2021	1550	68	M	Hemicolectomy	Descending colon	Adenocarcinoma	Well differentiated	Ulceroproliferative	T3N1bMx	IIIB	>50mm	2	Absent	Absent	6
82	35236	2021	1830	60	F	Hemicolectomy	Ascending colon	Adenocarcinoma	Well differentiated	Ulceroproliferative	T3N0Mx	IIIA	>50mm	0	Absent	Absent	5
83	40225	2021	1951	55	F	APR	Rectum	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T3N0Mx	IIA	<50mm	0	Absent	Absent	3
84	48038	2021	2174	70	F	Hemicolectomy	Descending colon	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T2N0Mx	I	<50mm	0	Absent	Absent	2
85	46320	2021	2188	60	F	Hemicolectomy	Descending colon	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T2N1bMx	IIIA	>50mm	1	Absent	Absent	6
86	64673	2022	463	50	F	Hemicolectmy	Descending colon	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T4aN2bMx	IIIC	>50mm	11	Present	Absent	4
87	50567	2022	574	56	M	Hemicolectmy	Descending colon	Adenocarcinoma	Well differentiated	Infiltrative	T4aN1cMx	IIIB	<50mm	3	Present	Absent	6
88	71096	2022	684	53	M	Hemicolectmy	Rectum	Adenocarcinoma	Moderately differentiated	Proliferative	T3N0Mx	II	>50mm	0	Absent	Absent	3
89	77098	2022	837	60	F	APR	Rectum	Adenocarcinoma	Moderately differentiated	Infiltrative	T4bN1cMx	IIIC	>50mm	1	Absent	Absent	4
90	76836	2022	863	54	M	Hemicolectmy	Rectosigmoid junction	Adenocarcinoma	Well differentiated	Infiltrative	T3N0Mx	IIA	>50mm	0	Absent	Absent	5
91	63632	2022	884	76	F	Hemicolectmy	Transverse colon	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T3N2aMx	IIIB	>50mm	1	Present	Absent	4
92	78366	2022	972	50	M	Hemicolectmy	Transverse colon	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T3N1Mx	IIIB	>50mm	1	Present	Absent	5
93	84786	2022	1160	72	F	Total colectomy	Caecum	Mucinous Adenocarcinoma	Well differentiated	Infiltrative	T2N2aMx	IIIB	>50mm	5	Absent	Absent	4
94	112259	2022	1782	52	M	Hemicolectmy	Transverse colon	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T2N0Mx	I	>50mm	0	Absent	Absent	5
95	122885	2022	1815	85	M	Hemicolectmy	Descending colon	Adenocarcinoma	Moderately differentiated	Ulceroproliferative	T3N1aMx	III	<50mm	1	Absent	Absent	4