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Original Article

Pathology Section

Immunohistochemical Expression Profile of SATB2 in Colorectal Adenocarcinoma and Association with Clinicopathological Parameters

M SUVAITHA[1], CD ANAND[2], JAISON JACOB JOHN[3]

ABSTRACT

Introduction: Colorectal carcinoma is the third most common cancer worldwide. Several clinicopathological parameters act as prognostic factors in colorectal carcinoma, but only a few are helpful in predicting the treatment outcome. Therefore, there is a need for better prognostic markers which also aids in assessing treatment benefits in colorectal carcinoma patients. Special AT Rich Sequence Binding Protein 2 (SATB2) is a highly specific marker for colorectal tissue. Decreased expression of SATB2 is also associated with poor prognosis in colorectal carcinoma.

Aim: To analyse the histomorphology, immunohistochemical expression profile of SATB2 and association with clinicopathological parameters in colorectal adenocarcinoma.

Materials and Methods: The cross-sectional study included 84 cases of colorectal carcinoma received in the Department of Pathology, SRM Medical College Hospital and Research Centre, Kattankulathur, Chennai, Tamil Nadu, India, in the period between April 2021 to September 2022. Both biopsy and resected specimens were included in the study. Relevant clinical data was collected. Histological diagnosis, grading and staging of the tumour was done using Haematoxylin and Eosin (H&E) slides as described and tabulated. Immunohistochemistry (IHC) for SATB2 was done and expression profile compared with the clinicopathological parameters to assess prognostic significance. Data was analysed using software-Statistical Package for Social Sciences (SPSS, version 23.0).

Results: Out of the 84 cases, 42 were biopsy and 42 were resected specimens. Mean age of the patients in the study was 57.9 years. Patients were predominantly males (n=51, 60.7%) with a male:female ratio of 1.54:1. Of the 84 cases, 40.5% (n=34) had tumour located in the rectum. Majority of the cases were moderately differentiated adenocarcinoma (n=48, 57.1%). Predominantly, stage III tumours (n=33, 39.3%) were noted. Out of the tumours showing decreased expression of SATB2, 55% (n=22) were left-sided tumours, metastasis was seen in 60% (n=24 cases), 37.5% of cases (n=9) showed lymphovascular invasion, and 55% (n=22) had a stage III tumour.

Conclusion: The present study results indicate that a decrease in SATB2 expression is associated with presence of lymphovascular invasion, perineural invasion, regional and distant metastasis and a higher pathological stage which signifies poor prognosis in colorectal carcinoma. These aid the physician for risk stratification of patients and enable personalised treatment choices including adjuvant chemotherapy in high-risk groups.

Keywords: Carcinoma, Metastasis, Prognosis, Special AT rich sequence binding protein 2

INTRODUCTION

Colorectal Carcinoma is the third most common cancer in the world and the second most common cancer in terms of mortality. There is an increase in the incidence with around 1.9 million new cases and 9,35,000 mortalities of CRC in 2020 [1]. Early detection of the tumour, adequate surgical removal and appropriate adjuvant therapy are of paramount importance to achieve a favourable outcome. At present, the pathological stage of the tumour at the time of presentation is the most essential prognostic factor in colorectal carcinoma. Although many studies are being done to determine the molecular markers which aid in identifying the cases at high-risk, and helps to choose the patients for adjuvant therapy, none of them have been proved to be good enough for routine clinical use.

SATB2, an epigenetic regulator and a nuclear matrix associated transcription factor, was initially recognised to be involved in craniofacial and osteoblast differentiation in humans. Later, it was discovered to be a highly tissue specific protein being expressed predominantly in the glandular cells of lower gastrointestinal tract [2]. This was further proved by various studies that SATB2 is a useful and a specific diagnostic marker to differentiate tumours of colorectal origin from other tumours, such as that of ovarian and pancreatic origin [3].

SATB2, besides being a diagnostic marker, was shown to have prognostic significance in colorectal carcinoma by few other studies [2,4,5]. Disease progression in colorectal carcinoma is associated with tumour invasion and metastasis which determines prognosis, it is therefore essential to recognise the role of genes and its associated proteins involved in tumour progression [4]. Decreased SATB2 expression is found to be associated with metastasis and poor prognosis in colorectal carcinoma, suggesting that loss of SATB2 may be involved in the progression of the tumour.

Study objectives:

- To study the various histomorphological patterns of colorectal carcinoma and categorise them according to World Health Organisation (WHO) classification, 2019 [6].
- To do clinicopathological correlation of SATB2 expression, its association with clinicopathological parameters and assess its prognostic value in colorectal carcinoma.

The SATB2 expression in colorectal carcinoma has not been studied in Indian population so far and its impact on prognostic parameters is still not established. Hence, analysing this protein expression and clinicopathological association could be a valuable tool for personalised treatment options for the patients.

MATERIALS AND METHODS

The study is a cross-sectional study carried out at the Department of Pathology, SRM Medical College Hospital and Research Centre, Kattankulathur, Chennai, Tamil Nadu, India. Scientific and Ethical committee approval was obtained (Ethical approval number: 2428/IEC/2021). Study period was from April 2021 to September 2022. A total of 84 cases of colorectal carcinoma was included in the study.

Inclusion criteria:

- All cases of colorectal biopsies diagnosed as adenocarcinoma.
- All colectomy specimens including right and left hemicolectomy, low anterior resection, abdominoperineal resection and total colectomy specimens received in the histopathology section of department of pathology.

Exclusion criteria:

- Superficial biopsies where representative material is not available.
- Cases for which material is inadequate.
- Postchemotherapy colectomy specimens with no significant residual tumour.

Study Procedure

The detailed clinical data with clinicopathological variables like age, gender, clinical presentation, Carcinoembryonic antigen (CEA) levels (≥5 ng/mL was suggestive of disease progression and worse prognosis) [7] were collected from the medical records department.

Grossing and processing of the specimens was carried out using routine protocol. The H&E slides were studied for tumour morphology, histological subtype, differentiation and grading, depth of invasion, lymphovascular invasion, perineural invasion, lymph node metastasis and Tumor (T), Nodes (N), and Metastases (M), (TNM) staging [6]. The cases were categorised according to the WHO classification of tumours of colorectum [6].

Immunohistochemistry (IHC): Peroxidase-Antiperoxidase system. Tissue Sections (4-5 µ) were made on rotary microtome (*Leica*: RM2125 RTS, Germany). Positively charged slides (Path In-Situ: PS-011-72; India) were used for taking the sections for IHC procedure. Antigen retrieval on tissue sections was done by microwave method (800 W×7 minutes, 640 W×7, 640 W×7 minutes; Samsung (India) microwave-Model-MC32K7056CK).

Immunohistochemical staining was done on sections using the following primary and secondary antibody and detection system.

Primary Antibodies for IHC from Path In-Situ (India) as below: SATB2 (rabbit monoclonal; Clone EP281; Catalogue No. PR239-3 mL RTU).

Secondary Antibody and Detection system from Path In-Situ (India) as below: Poly-excel HRP (Horse Radish Peroxidase)/DAB (3,3'-diaminobenzidine) Detection System-Two Step; Catalogue No. PEH002-6 mL.

Grading of IHC expression- SATB2: The results of the IHC stains were evaluated manually and scored semi-quantitatively as a sum of proportion and intensity of the nuclear stain. Two pathologists evaluated the IHC slides by microscopy and graded the expression to avoid inter-observer variation. There was substantial agreement between the two pathologists with a kappa value of 0.68. The scoring of SATB2 was done as per criteria described by Magnusson K et al., and summarised in [Table/Fig-1] [8]. Based on the previous study, for statistical analysis, a final SATB2 staining score of >=3 was taken as positive and <3 as negative [5]. Both extent and intensity of the staining was taken into account for result analysis.

STATISTICAL ANALYSIS

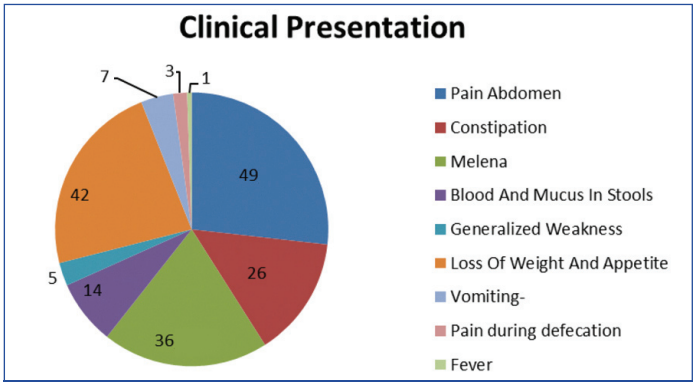
Data was analysed using software-Statistical Package for Social Sciences (SPSS, version 23.0). Descriptive data like percentage and frequency were calculated. The comparison and association between different clinicopathological parameters and SATB2 expression was demonstrated using Chi-square test at 5% level of significance, a probability of value <0.05 was considered significant.

Extent of nuclear staining	Score
0-1%	0
2-25%	1
26-75%	2
>75%	3
Intensity of nuclear staining	**Score**
Negative	0
Weak	1
Moderate	2
Strong	3

[Table/Fig-1]: SATB2 scoring [5].

RESULTS

The present study comprised of 84 cases of colorectal carcinoma, out of which 42 were biopsies and 42 were resected colectomy specimens. The distribution of clinical symptoms in the study population is summarised in [Table/Fig-2]. The most common presenting symptom was abdominal pain seen in 49 (58.3%) cases of cases, followed by loss of weight and appetite 42 (50%) cases, melaena 36 (42.9%) cases, constipation 26 (30%) cases and presence of blood and mucus in stools 14 (16.7%) cases.



[Table/Fig-2]: Distribution of the clinical symptoms in the study participants.

The age group of the study participants ranged from 22-86 years with a mean age of 57.9 years and majority of them were males (n=51, 60.7%) with a male to female ratio of 1.5:1 [Table/Fig-3]. A precursor lesion was present in 25% (n=21) of the cases which was an adenomatous polyp in all the cases. CEA levels were available for only 32 cases from the past records of patients out of which, high CEA level (>5 ng/mL) was seen in 22 cases (26.2%), and the remaining 10 cases had low CEA levels (<5 ng/mL) [Table/Fig-3].

Clinico pathological parameter	SATB2 Positive (n=44)	SATB2 Negative (n=40)
Age		
<50 years	7	12
>50 years	37	28
Sex		
Males	23	24
Females	21	16
Precursor lesion		
Present	5	7
Absent	13	17
CEA levels		
High (>5 ng/mL)	12	10
Low (<=5 ng/mL)	8	2
Not available	24	28

Tumour side		
Right-sided	12	18
Left-sided	32	22
Metastasis		
Present	12	24
Absent	32	16
Differentiation/Grading		
Well-differentiated (G1)	16	6
Moderately differentiated (G2)	28	30
Poorly differentiated (G3)	0	4
Stage I	14	5
Stage II	15	9
Stage III	11	22
Stage IV	4	4
LVI (n=42 resected specimens)	(n=18)	(n=24)
Present	2	9
Absent	16	15
PNI (n=42 resected specimens)	(n=18)	(n=24)
Present	1	3
Absent	17	21

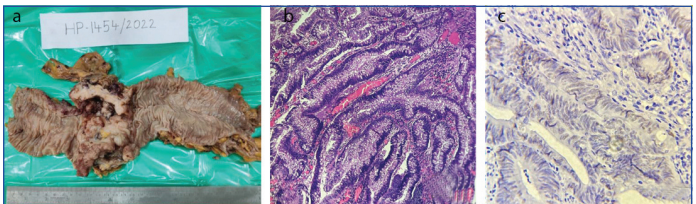
[Table/Fig-3]: SATB2 results compared with various clinicopathological parameters. *LVI: Lymphovascular invasion; PNI: Perineural invasion; All relevant data has been included in the table

The lesion was most commonly left-sided seen in 64.3% (n=54) of the cases, and right-sided lesion was seen in 30 cases (35.7%). The most common site was the rectum seen in 40.5% of the cases (34 cases), followed by the ascending colon in 22.6% (n=19) of the subjects while in 15.5% (n=13) of the participants, it is the rectosigmoid. Only one subject had lesion in splenic flexure [Table/Fig-3]. On assessing the gross morphology of the tumour in the 42 resected specimens, Majority of the tumours (52.4%, 22 cases) were ulceroproliferative type, followed by proliferative (16.6%, 7 cases), polypoidal (14.3%, 6 cases), napkin ring constriction (9.5%, 4 cases), fungating growth (4.8%, 2 cases) and a cystic swelling (2.4%, 1 case) in decreasing order of frequency [Table/Fig-4].

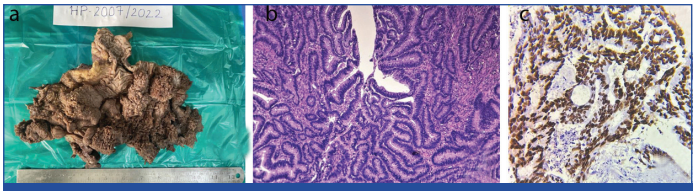
Variables	Frequency (n)	Percentage (%)
Polypoidal	6	14.3
Ulceroproliferative	22	52.4
Napkin ring constriction	4	9.5
Proliferative	7	16.6
Cystic swelling	1	2.4
Fungating growth	2	4.8
Total	42	100

[Table/Fig-4]: Gross morphology of the tumour.

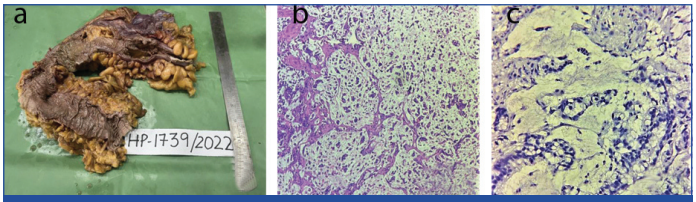
Of all the 84 cases of colorectal carcinoma, 57.1% (n=48) of cases were moderately differentiated adenocarcinoma [Table/Fig-5], 26.2% (n=22) was well-differentiated adenocarcinoma [Table/Fig-6], 11.9% (n=10) Mucinous adenocarcinoma [Table/Fig-7] and 4.8% (n=4) signet ring adenocarcinoma.



[Table/Fig-5]: Moderately differentiated adenocarcinoma. (a) Gross, showing an ulceroproliferative growth in the splenic flexure of the colon; (b) H&E (10X), tumour cells are arranged in glandular and papillary pattern with fibrovascular cores; (c) IHC SATB2 (40X), showing a score 3 {weak staining in about 50% of the cells (1+2)}.



[Table/Fig-6]: Well-differentiated adenocarcinoma. (a) Gross: showing a proliferative growth in the Rectosigmoid; (b) H&E (10X) showing tumour cells arranged in glandular pattern; (c) IHC SATB2 (40X), showing a score 5 (moderate staining in >75% of the cells).



[Table/Fig-7]: Mucinous carcinoma. (a) Gross-showing a napkin ring constriction in the descending colon; (b) H&E (10x), tumour cells arranged as small islands and as single cells among the extracellular lakes of mucin; (c) SATB2 (40x), shows a score 0, absent nuclear staining in all the cells.

Out of the 42 resected specimens, 25 cases showed a tumour depth of invasion upto the subserosal connective tissue, 14 cases showed invasion into the muscularis propria, and three cases showed serosal invasion. Of the 84 cases, metastasis (including both regional and distant metastasis) was seen in 43% of the cases (n=36), of which the most common was regional lymphnode metastasis seen in 33.3% (n=24) of cases. Lymph node metastasis and omental deposit was seen in 4.8% (n=4) of the subjects, metastasis was absent in 57.1% (n=48) of the cases [Table/Fig-8].

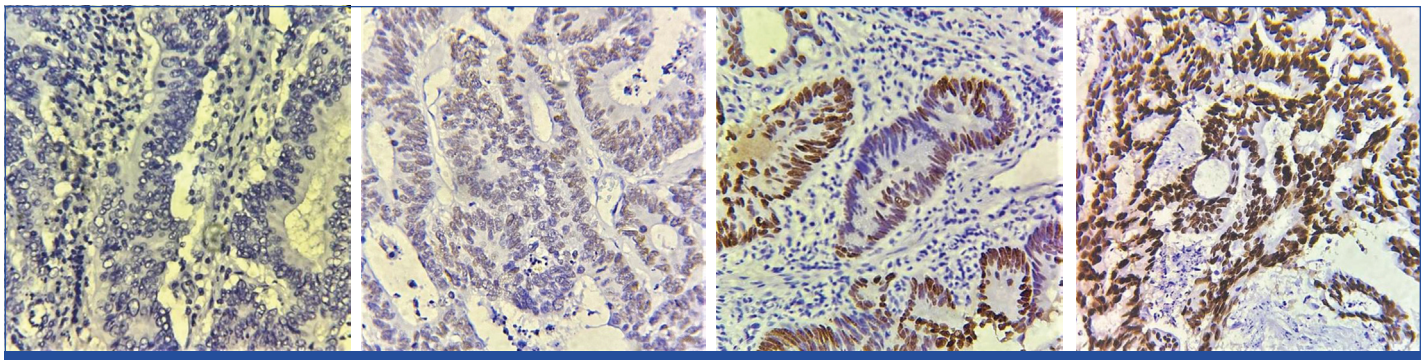
Metastasis	Frequency (n)	Percentage (%)
Absent	48	57.1
Lymph node metastasis	24	28.6
Lymph node metastasis, omental deposit	4	4.8
Lymph node metastasis, liver metastasis	1	1.2
Omental deposit	3	3.6
Liver metastasis	2	2.4
Liver metastasis, lung metastasis	1	1.2
Pouch of douglas	1	1.2
Total	84	100.0

[Table/Fig-8]: Sites of tumour metastasis.

Around 39.3% (n=33) had stage III carcinoma while 9.5% (n=8) had stage IV carcinoma. Stage I and II was seen in 22.6% (n=19) and 28.6% (n=24) cases, respectively [Table/Fig-3]. Out of the 34 patients who were under follow-up for a period of 18 months, there was one patient with tumour recurrence and two patients with death from disease, the remaining 31 cases were under chemotherapy and regular follow-up with routine scans and follow-up CEA levels and were doing good.

SATB2 expression results: SATB2 expression in colorectal carcinoma tissue was scored from 0 to 6 as per criteria described in [Table/Fig-1]. Majority of the cases (26 cases; 31%) in the present study showed a score of 0, followed by score 5 in 25% (n=21), score 4 in 15.5% of cases (n=13), score 2 in 14.3% cases (n=12), score 3 in 8.3% cases (n=7), score 6 in 3.6% cases (n=3), and score 1 in 2.4% cases (n=2). SATB2 scoring was further categorised into positive score (more than or equal to three) and negative score (less than three). Positive SATB2 score was seen in 44 cases (52.3%) and negative score was seen in 40 cases (47.7%). The various range of SATB2 scores (0 to 6) are illustrated in [Table/Fig-9-12], respectively.

On comparison of SATB2 scores with various study parameters [Table/Fig-3]. Out of 40 SATB2 negative cases, 10 cases (25%) were associated with high CEA levels, and two cases has low CEA levels with a p-value 0.142 [Table/Fig-13].



[Table/Fig-9]: SATB2 score 0 (absent nuclear staining in all the cells), moderately differentiated adenocarcinoma. **[Table/Fig-10]:** SATB2 score 4 {weak staining in >75% of cells, (1+3=4)}. **[Table/Fig-11]:** SATB2 score 4 {weak staining in >75% of cells, (1+3=4)}. **[Table/Fig-12]:** SATB2 score 4 {weak staining in >75% of cells, (1+3=4)}. (Images from left to right)

CEA levels	SATB2		Total	p-value
	<3	>=3		
High	10 (25%)	12 (27.2%)	22	0.142
Low	2 (5%)	8 (18.2%)	10	
NA	28 (70%)	24 (54.5%)	52	
Total	40	44	84	

[Table/Fig-13]: Comparison of CEA levels of the study participants with SATB2 score.

Of the 40 cases with a negative SATB2 score, 22 (55%) cases were left-sided and 18 (45%) cases were right-sided with a significant p-value of 0.030 [Table/Fig-14]. Among the 40 SATB2 negative cases, the current study showed 55% (n=22) cases of moderately differentiated adenocarcinoma, 20% (n=8) mucinous adenocarcinoma, 15% (n=6) well-differentiated adenocarcinoma, and 10% (n=4) signet ring adenocarcinoma [Table/Fig-15]. Comparison of histologic subtype and SATB2 using Chi-square analysis shows that it is statistically significant with a p-value of 0.006.

Side	SATB2		Total	p-value
	<3	>=3		
Left	22 (55%)	32 (72.7%)	54	0.030
Right	18 (45%)	12 (27.3%)	30	
Total	40	44	84	

[Table/Fig-14]: Comparison of the SATB2 score with the side of the lesion.

Histologic subtype	SATB2		Total	p-value
	<3	>=3		
Well-differentiated adenocarcinoma	6 (15%)	16 (36.3%)	22	0.006
Moderately differentiated adenocarcinoma	22 (55%)	26 (59.1%)	48	
Signet ring adenocarcinoma	4 (10%)	0	4	
Mucinous adenocarcinoma	8 (20%)	2 (4.5%)	10	
Total	40	44	84	

[Table/Fig-15]: Histological subtype and SATB2 expression.

Of the 40 SATB2 negative cases; 24 (60%) cases showed the presence of metastasis and in 16 (40%) cases there was no metastasis. Out of the 24 cases which showed metastasis, 17 cases (42.5%) showed only lymphnode metastasis; lymph node metastasis and omental deposit, only omental deposits and only liver metastasis were seen in 2 cases (5%) each; and 1 case (2.5%) showed liver and lung metastasis [Table/Fig-16]. Comparison of metastasis and SATB2 using chi-square analysis shows that it is statistically significant with a p-value of 0.042.

Out of the SATB2 negative cases, majority of the cases 22 (55%) were stage III, followed by 9 cases (22.5%) of stage II , 5 cases (12.5%) stage I and 4 cases (10%) stage IV with a p-value of 0.026 [Table/Fig-17].

Lymphovascular invasion and perineural invasion was assessed with the SATB2 expression results in the 42 resected specimens. Out of these 42 cases, 24 cases (57%) were SATB2 negative and

Metastasis	SATB2		Total	p-value
	<3	>=3		
Absent	16 (40%)	32 (72.7%)	48	0.042
Lymph node metastasis	17 (42.5%)	7 (15.9%)	24	
Lymph node metastasis and omental deposit	2 (5%)	1 (2.3%)	3	
Lymph node metastasis and liver metastasis	0	1 (2.3%)	1	
Omental deposit	2 (5%)	1 (2.3%)	3	
Liver metastasis	2 (5%)	0	2	
Liver and lymph node metastasis	0	1 (2.3%)	1	
Liver and lung metastasis	1 (2.5%)	0	1	
Pouch of douglas	0	1 (2.3%)	1	
Total	40	44	84	

[Table/Fig-16]: Comparison of SATB2 expression with metastasis.

Final stage	SATB2		Total	p-value
	<3	>=3		
I	5 (12.5%)	14 (31.8%)	19	0.026
II	9 (22.5%)	15 (34.1%)	24	
III	22 (55%)	11 (25%)	33	
IV	4 (10%)	4 (9.1%)	8	
Total	40	44	84	

[Table/Fig-17]: Comparison of SATB2 expression with the pathological stage of the tumour.

18 cases (43%) were SATB2 positive. Out of the 24 SATB2 negative cases, lymphovascular invasion was present in 9 (37.5%) cases; whereas out of the 18 SATB2 positive cases, lymphovascular invasion was absent in 16 (88.8%) cases [Table/Fig-18], which showed statistical significance with a p-value of 0.045. In the present study, perineural invasion was seen in four cases, out of which three cases had a negative SATB2 expression and only one case showed a positive SATB2 expression. Comparison of perineural invasion and SATB2 using chi-square analysis shows that it is not statistically significant with a p-value of 0.45 [Table/Fig-19].

Lymphovascular invasion	SATB2		Total	p-value
	<3	>=3		
Absent	15 (62.5%)	16 (88.9%)	31	0.045
Present	9 (37.5%)	2 (11.1%)	11	
Total	24	18	42	

[Table/Fig-18]: Comparison of the presence of lymphovascular invasion with SATB2.

Perineural invasion	SATB2		Total	p-value
	<3	>=3		
Absent	21 (87.5%)	17 (94.4%)	38	0.45
Present	3 (12.5%)	1 (5.6%)	4	
Total	24	18	42	

[Table/Fig-19]: Comparison of the presence of perineural invasion and SATB2 score.

DISCUSSION

Many of the cases of colorectal carcinomas have been characterised by delayed onset of symptoms and variable rates of progression leading to few cases being diagnosed at an advanced stage [1-5]. Many studies have established the use of newly discovered molecular markers in assessing the prognosis of the disease and in appropriate patient management [2,5]. The identification of new molecules and proteins involved in the pathophysiology and step-wise progression of colorectal carcinoma helps to assess prognostic significance and to identify new therapeutic targets for the disease.

In the present study, on SATB2 expression in colorectal carcinomas, the mean age and gender distribution matched with the studies of Wang S et al., and Zhang YJ et al., respectively [5,9]. Eighteen cases (21.4%) in the present study had an early onset colorectal carcinoma (age <50 years). Out of these 18 cases, 7 (39%) were females and 11 (61%) were males.

Out of the 18 cases, 5 (28%) were right-sided and 13 (72%) were left-sided which is a newly developing fact in literature. Abdominal pain being the most common symptom in the present study matched with the study of Kaplan MA et al., who observed the clinicopathological characteristics of colorectal carcinoma [10]. Most of the cases with high CEA levels in the present study showed a higher stage which was comparable to the study of Ramphal W et al., [7]. However, the comparison of follow-up CEA levels in the present study could not be done. Majority of the cases (64.3%) in the present study were left-sided which matched with the other studies in literature.

On gross evaluation of the cases in the present study, 22 cases (52.4%) showed an ulceroproliferative growth, our observation was consistent with the study of Park YJ et al., who also found that ulceroproliferative growth was the most common gross morphological pattern in their study [11]. All the four cases showing napkin ring constriction in the present study were left-sided which was a consistent feature as per literature.

SATB2 and clinicopathological parameters (age, sex, tumour grade, stage, lymph node metastasis, CEA levels, tumour site, histological type, lympho vascular invasion, perineural invasion). In the present study, among the SATB2 positive cases, 30 cases (68%) were males and 14 cases (32%) were females; and most of the patients were above 50 years of age, except four patients in the age group of 30-50 years, out of which one was female and three were males. Among the SATB2 negative cases, 24 (60%) were males and 16 cases (40%) were females. The youngest patient among our study was 22 years female patient, who showed SATB2 negative score. She had a stage III moderately differentiated tumour in the rectum, with lymph node metastasis. There was no associated precursor lesion in that patient. These findings were in consistent with literature which proved that early onset colorectal carcinoma is associated with a poor prognosis.

Out of the 40 SATB2 negative cases, 10 cases (83%) were associated with high CEA levels, which was in concordance to the study of Wang S et al., which showed high CEA levels in 44.3% of SATB2 negative cases [5]. However, the value in the present study was not statistically significant. Decreased expression of SATB2 is seen slightly more commonly in left-sided tumours (55%) than right-sided tumours (45%). In the previous studies done by Wang S et al., Li J et al., and Eldeeb SA et al., the incidence of SATB2 negativity in left-sided tumours range from 57%-82% and 18-43% in right-sided tumours [5,12,13]. The prognostic significance of the differential expression of SATB2 in the right and left-sided cancers should be considered and further studies are required to find out the actual biological properties of these tumours with respect to side.

The present study also showed an inverse association between SATB2 expression and the presence of metastasis, which is associated with an unfavourable outcome in patients. Similar results were also seen in the studies done by Liu F et al., Wang S et al., Li J et al., and Eldeeb SA et al., [3,5,12,13]. Most of the mucinous adenocarcinomas and all the cases of signet ring adenocarcinoma in this study were SATB2 negative. This was consistent with the results of Liu F et al., Eldeeb SA et al., Ma C et al., [3,13,14]. These tumours also showed a predilection to the right colon which is a wellknown fact as per literature.

Decreased expression of SATB2 was associated with a higher stage and lymphovascular invasion which also showed statistical significance. This was also shown in the previous studies done by Li J et al., Eldeeb SA et al., Ma C et al., [12-14]. It is also a known fact that higher stage and lymphovascular invasion is associated with a poor prognosis. Therefore, SATB2 can be used as an independent prognostic factor for disease outcome.

Earlier studies by Yang Y et al., and Liebig C et al., have proved the presence of perineural invasion as an independent prognostic factor in colorectal carcinoma [15,16]. In the present study, perineural invasion was seen in four cases, out of which three cases had a negative SATB2 expression and only one case showed a positive SATB2 expression which is in concordance with the studies of Li J et al., and Eldeeb SA et al., [12,13]. However, this was not found to be statistically significant.

Based on the above observances in the present study, authors found that decreased SATB2 expression is associated with poor prognosis which is indicated by presence of metastasis, lymphovascular invasion, perineural invasion, higher tumour stage in the cases. Follow-up was available for only 34 cases and was done only for 18 months. However, additional follow-up of more patients for extended periods of time would be needed to prove the prognostic outcome.

Limitation(s)

Poorly differentiated colonic adenocarcinoma was not represented in the present study population except signet ring carcinoma and the study with more number of cases would have helped us reach more statistically significant conclusions and follow-up data on all cases was not available. Only 34 cases were available for follow-up.

CONCLUSION(S)

In the present study, decreased expression of SATB2 is associated with regional and distant metastasis, presence of lymphovascular invasion, perineural invasion, a higher tumour grade and a higher pathologic stage of the tumours at the time of diagnosis all of which are indicator of poor prognosis. Hence, the present study indicates that diminished expression of SATB2 in the tumour cells is associated with poor prognosis in colorectal carcinoma. This can aid in patient stratification and enable personalised treatment approaches for best outcome and quality of life for patients.

REFERENCES

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2021;71(3):209-49.
[2] Eberhard J, Gaber A, Wangefjord S, Nodin B, Uhlen M, Ericson Lindquist K, et al. A cohort study of the prognostic and treatment predictive value of SATB2 expression in colorectal cancer. British Journal of Cancer. 2012;106(5):931-38.
[3] Liu F, Gao Z, Shen D, Zhao H, Wang C, Ye Y, et al. Significance of SATB2 expression in colon cancer and its differential diagnosis in digestive tract adenocarcinoma and ovarian primary and metastatic carcinoma. Pathology-Research and Practice. 2019;215(7):152430.
[4] Cígerová V, Adamkov M, Drahošová S, Grendar M. Immunohistochemical expression and significance of satb2 protein in colorectal cancer. Annals of Diagnostic Pathology. 2021;52:151731.
[5] Wang S, Zhou J, Wang XY, Hao JM, Chen JZ, Zhang XM, et al. Down-regulated expression of SATB2 is associated with metastasis and poor prognosis in colorectal cancer. The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland. 2009;219(1):114-22.

[6] International Agency for Research on Cancer, World Health Organization, International Academy of Pathology. WHO classification of tumours. Digestive system tumours: WHO classification of tumours, volume 1. 1st ed. Elder DE, editor. IARC; 2019.
[7] Ramphal W, Boeding JR, van Iwaarden M, Schreinemakers JM, Rutten HJ, Crolla RM, et al. Serum carcinoembryonic antigen to predict recurrence in the follow-up of patients with colorectal cancer. The International Journal of Biological Markers. 2019;34(1):60-68.
[8] Magnusson K, de Wit M, Brennan DJ, Johnson LB, McGee SF, Lundberg E, et al. SATB2 in combination with cytokeratin 20 identifies over 95% of all colorectal carcinomas. The American Journal of Surgical Pathology. 2011;35(7):937-48.
[9] Zhang YJ, Chen JW, He XS, Zhang HZ, Ling YH, Wen JH, et al. SATB2 is a promising biomarker for identifying a colorectal origin for liver metastatic adenocarcinomas. E Bio Medicine. 2018;28:62-69.
[10] Kaplan MA, Ozaydin S, Yerlikaya H, Karaagac M, Gumus M, Cil T, et al. Clinicopathologic and prognostic differences between three different age groups (child/adolescent, young adults, and adults) of colorectal cancer patients: A multicentre study. Oncology Research and Treatment. 2019;42(10):516-22.
[11] Park YJ, Park KJ, Park JG, Lee KU, Choe KJ, Kim JP. Prognostic factors in 2230 Korean colorectal cancer patients: Analysis of consecutively operated cases. World Journal of Surgery. 1999;23(7):721-26.
[12] Li J, Zeng Q, Huang H, Qin X, Chen L. Loss of SATB2 and CDX2 expression is associated with DNA mismatch repair protein deficiency and BRAF mutation in colorectal cancer.
[13] Eldeeb SA, Salem MM, Morsi DF, Soliman NA. Immunohistochemical expression of SATB2 and clinicopathological correlation in colorectal adenocarcinoma. Merit Res J Med Med Sci. 2022;10(4):115-24.
[14] Ma C, Olevian D, Miller C, Herbst C, Jayachandran P, Kozak MM, et al. SATB2 and CDX2 are prognostic biomarkers in DNA mismatch repair protein deficient colon cancer. Modern Pathology. 2019;32(8):1217-31.
[15] Yang Y, Huang X, Sun J, Gao P, Song Y, Chen X, et al. Prognostic value of perineural invasion in colorectal cancer: A meta-analysis. Journal of Gastrointestinal Surgery. 2015;19(6):1113-22.
[16] Liebig C, Ayala G, Wilks J, Verstovsek G, Liu H, Agarwal N, et al. Perineural invasion is an independent predictor of outcome in colorectal cancer. Journal of Clinical Oncology. 2009;27(31):5131.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Resident, Department of Pathology, SRM Medical College Hospital and Research Centre, Faculty of Medical and Health Sciences, SRMIST, Katt Chennai, Tamil Nadu, India.
2. Professor, Department of Pathology, SRM Medical College Hospital and Research Centre, Faculty of Medical and Health Sciences, SRMIST, Katt Chennai, Tamil Nadu, India.
3. Professor and Head, Department of Pathology, SRM Medical College Hospital and Research Centre, Faculty of Medical and Health Sciences, SRMIST, Katt Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Jaison Jacob John,
Professor and Head, Department of Pathology, SRM Medical College Hospital,
SRM Nagar, Potheri Village, Kattankulathur, Chennai, Tamil Nadu, India.
E-mail: pathologysrmktr@gmail.com

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