Role Of Mean Platelet Volume In Prognosis Of Gall Bladder Carcinoma –A Tertiary Centre Experience

BASAVEGOWDA VINOD PRAKASH, PAVAN JONNADA , ALI ZAID ANWAR , RAGHAVENDRA HARSHA , PRAVEEN ARAKERI ,
1ASSOCIATE PROFESSOR, 2senior reisdent, 3JUNIOR RESIDENT, 4RESIDENT, 5RESIDENT
1KIDWAI MEMORIAL INSTITUTE OF ONCOLOGY,
2KIDWAI MEMORIAL INSTITUTE OF ONCOLOGY,
3KIDWAI MEMORIAL INSTITUE OF ONCOLOGY,
4KIDWAI MEMORIAL INSTITUTE OF ONCOLOGY ,
5KIDWAI MEMORIAL INSTITUE OF ONCOLOGY

ABSTRACT

The mean platelet volume (MPV) is an inflammatory marker which suggest the activation Platelets .There are number of studies which suggest the association between the neoplastic process and metastasis of cancer . Here we have conducted a retrospective analysis to find the role of MPV as a prognostic informative marker in gall bladder cancer

This study includes a retrospective analysis of 73 patients with gall bladder cancer who Underwent treatment for gall bladder cancer with curative or palliative intent . MPV was obtained and statistically analysed to find association between the nodal status (N) , overall stage as per American Joint Committee on Cancer (AJCC) staging system, perineural invasion and differentiation of the tumor ,using Statistical Package for the Social Sciences (SPSS) software (IBM corp. version 23).

It was seen in this study that MPV values were significantly high in nodal positive cases (OR 3.623 ,95% CI (7.778-1.687) ; p value -0.0001), advanced stage (OR 3.623 ,95 % CI (7.778-1.687) ; p value of 0.0001) , perineural invasion (OR 3.396 , 95 %CI (8.319-1.387) ; p value -0.0001) , poor differentiation (OR 2.327 , 95 % CI (4,651-1.164) ; p value -0.002).MPV is an inflammatory marker which relates the nodal positivity in staging and prognostication of gall bladder cancer . This marker is inexpensive and can be done conveniently aiding in ascertaining risk status of gall bladder cancer

Key words :-gall bladder cancer , mean platelet volume , diagnosis

INTRODUCTION

Gall bladder cancer has been found to be the most common cancer of the hepatobiliary system having an incidence of 1.2 % of total cancer diagnosis .It has been shown to account for about 165,087 death and 1.7 % of total cancer death as noticed in 2018 [1].

The presentation of gall bladder cancer is often confusing and causes delay in diagnosis. It is often discovered incidentally after a simple cholecystectomy or when it is at a very advanced stage causing ascites or jaundice [2]. It is often found to be unresectable with a dismal prognosis in stage I ,II , III , IV which were 60 % , 50% , 20-25% and 5 to 5-15 %.[3].

Surgery can provide complete cure in early stage of the disease , with simple cholecystectomy sufficing for in situ carcinoma or T1a , with more radical resection needed in advanced stage if possible where negative margin is to be obtained leading to resection of liver , bile ducts with local lymphadenectomy [3,4].

There has been a limited availability of tumor markers which can be employed in diagnosis of gall bladder cancer .The two most common markers which are commonly used are carcinoma embryonic antigen (CEA) and carbohydrate antigen(CA) 19-9[5] .Other markers which are not generally used are CA 15-3 ,CA 242 , Mac- 2BP but these have been found to have variable sensitivity and specificity[5,6] .

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MATERIALS AND METHODS

For this study we retrospectively analysed gall bladder cancer afflicted patients in kidwai memorial institute of oncology between January 2018 to January 2021. The data of seventy three patients was collected which included the staging of the patients under American joint committee on cancer (AJCC) recommendations , the histological characteristics of the tumor afflicting the patients form the computer database of the institute . The institutional review board clearance was obtained with appropriate consent .

For the analysis of MPV (mean platelet volume), the hemogram was obtained form the blood collected , about 5 to 10 ml from a peripheral vein into sterilized ethylenediaminetetraacetic acid (EDTA) tubes .The blood reports which were collected in the morning to minimize the circadian rhythm, and the value of MPV which was considered was the value at the time of diagnosis of the patient

The statistical analysis was performed with the usage of Statistical package for the Social Sciences (SPSS) software (IBM corp, version 23), the parameters were compared using mean and standard deviation . the parametric variables were compared using chi square analysis . A receiver-operating characteristic (ROC) curve analysis was performed to identify the optimal cut off values for MPV. A p value of <0.05 was considered to be significant .

RESULTS

This study included 73 patients of gall bladder cancer , there were 49 females and 24 males. The age range was from 38 to 82 years and the mean age was 60.2 .The other characteristic are presented in table 1.

Baseline characters	
Number of patients	73
males	24
females	49
Age range	38-82 years
Mean age	60.2 years
Mean platelet volume range	7.30-11.83 fl
Mean platelet volume (mean)	9.88 fl
AJCC STAGE 1	9
AJCC STAGE 2	11
AJCC STAGE 3	29
AJCC STAGE 4	24
poor differentiation	43
well,moderate differentiation	30
with perineural invasion	40
without perineural invasion	33

Table 1.

ROC curves were made to find an optimal cutoff of MPV value associated with lymph nodal positivity in gall bladder cancer patients . The area under curve amounted to 0.909 for MPV (FIGURE 1). The analysis revealed that MPV higher than 9.45 fl (femtolitre) indicates the positivity of lymph nodes with a sensitivity of 88% and specificity of 83%.
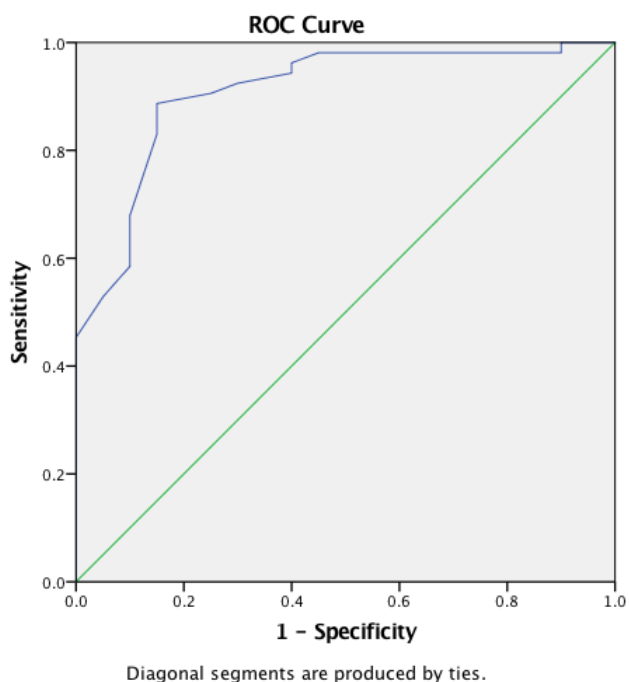

figure 1.:- ROC analysis showing MPV cut off .

The patients were then allotted into two groups one with low MPV (<9.4) and the other with high MPV(≥9.4).
It was seen in this study that MPV values were significantly high in nodal positive cases (OR 3.623 ,95% CI (7.778-1.687) ; p value -0.0001)as shown in figure 2 , advanced stage (OR 3.623 ,95 % CI (7.778-1.687) ; p value of 0.0001) as shown in figure 3 , perineural invasion (OR 3.396 , 95 %CI (8.319- 1.387) ; p value -0.0001) as shown in figure 4 , poor differentiation (OR 2.327 , 95 % CI (4,651-1.164) ; p value -0.002) as shown in figure 5. There was no significant association between high MPV and increase in age of sex of the patient . There was a negative association with high MPV and increased age or sex as shown in table 2.
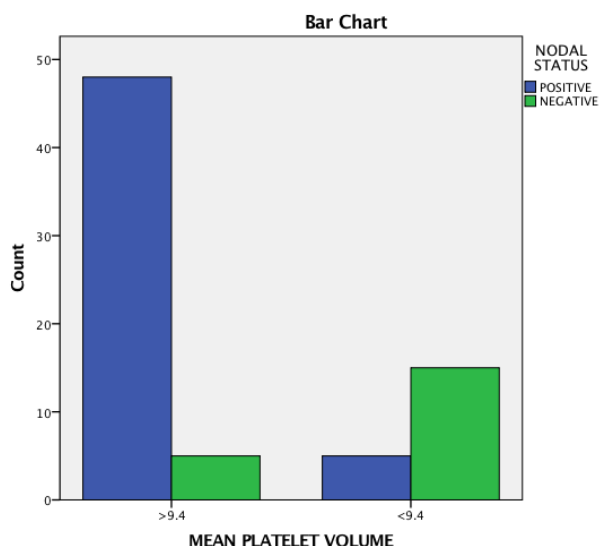

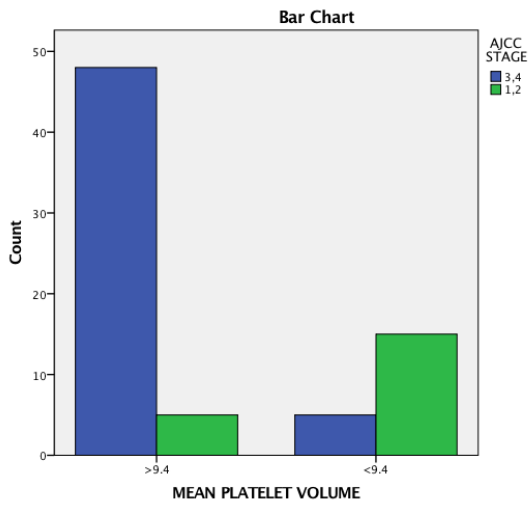figure 2:-relation between MPV and nodal status
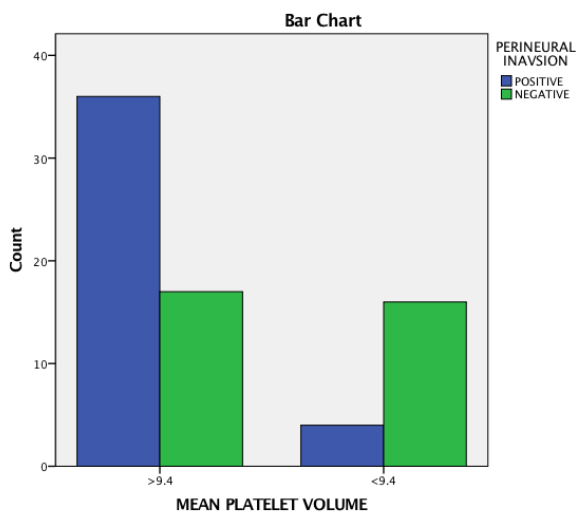
figure 3:- relation between ajcc stage and MPV

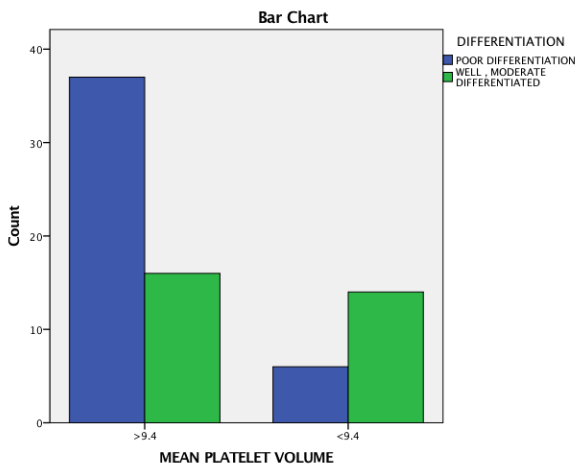figure 4:- relation between MPV and perineural invasion

FIGURE 5:- RELATION BETWEEN DIFFERENTIATION
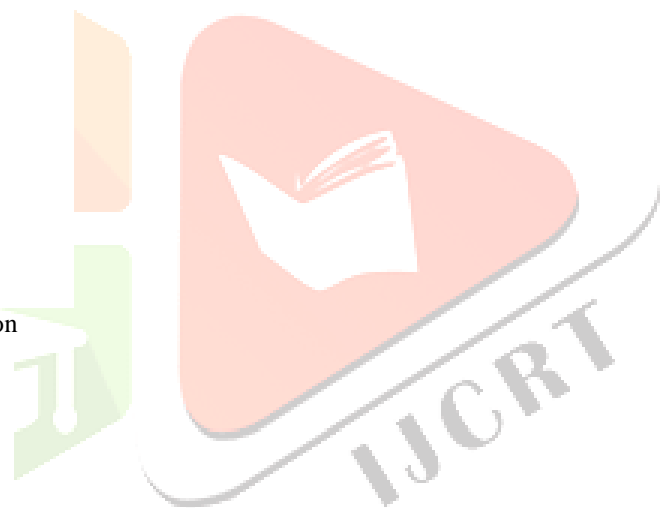
	patients	Low MPV(<9.4)	High MPV(≥9.4)	Chi square	P value	Odds ratio(95% CI)
gender				2.07	0.15	0.77(1.054-0.575)
male	24	5	19			
female	49	14	35			
Age				1.77	0.18	1.30(2.34-0.81)
<60 yrs	31	11	20			
>60 yrs	42	9	33			
AJCC stage				31.38	0.0001	3.623(7.778-1.687)
Stage 1,2	20	15	5			
Stage 3,4	53	5	48			
Nodal status				31.38	0.0001	3.623(7.778-1.687)
Node negative	20	15	5			
Node positive	53	5	48			
Perineural invasion				13.464	0.0001	3.396(8.319-1.387)
Perineural invasion present	40	4	36			
Perineural invasion absent	33	16	17			
Differentiation				9.507	0.002	2.327(4.651-1.164)
Poor differentiation	43	6	37			
Well, moderate differentiation	30	14	16			

Table 2 :- relationship between MPV and demographic and clinical parameters

DISCUSSION

In this study it has been seen that the increased value of MPV can reliably predict the involvement of lymph nodes in a case of gall bladder cancer . This research shows that MPV can be a prospective marker that aids even in prediction of advanced stage , perineural invasion , as well as poor differentiation histological character in cases of gall bladder cancer .

The increase in MPV values has been generally regarded as clumping of platelets as one of the features of inflammation processes which are undergoing , which enable the process of oncogenesis by generation of genetic material damaging agents like reactive oxygen species and promoting dissemination and invasion of cancer cells by production of chemokines and various other agents. The increase MPV can also lead to increased platelet depletion and it also indicates the immature platelets being released into circulation which are larger in size as compared to normal platelets [14].

In a number of different studies a correlation has been found between the presence of high MPV values in different cancers, MPV higher than 8.25 fl in cases of gastric carcinoma was found to be useful in monitoring patients for gastric carcinoma risk [11] . In cases of ovarian carcinoma the MPV value higher than 8.26 fl was found to be associated with worse tumor burden and prognosis [12].however in a study conducted by Sun SY et al[15]it was found that low values of MPV less than 8.10 fl was associated with worse prognosis in cases of esophageal carcinoma ,but in other studies conducted in cases of gastric carcinoma it was found that increased value of MPV greater than 10.2 fl was associated with worse prognosis and lymph node metastasis [16,17].

In this study a value of MPV greater than 9.4 fl was found to be associated with worse prognosis , including worse histological features and increased nodal dissemination as seen in similar study [13].

This study has the following limitations, as being retrospective in nature based on case records hence the detail pertaining to each case is limited in nature .In other aspect some patients underwent chemotherapy which may have influenced the attributes of the disease.

Hence in the present study there has been conclusively proven the association between increased MPV value and the local dissemination and prognosis of gall bladder cancer . Inspite of the fact that MPV has low specificity at low values ,this is a non invasive , inexpensive marker can be an invaluable addition to the present repertoire of tumor markers in risk stratification and predicting prognosis of gall bladder cancer

CONCLUSION

The evaluation and procuring of mean platelet volume is quick and inexpensive that in addition of being an inflammatory marker also helps in staging and risk assessment . The value of 9.4 fl has been found to be a cutoff for predicting nodal metastasis , advanced stage and worse histological features like poor differentiation and perineural invasion .Hence ,the inclusion of this parameter can aid in determining the prognosis of the disease.

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