VOLUME - 9, ISSUE - 9, September - 2020 • PRINT IS VOLUME - 9, ISSUE - 9, September - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Medicine

ROLE OF HSCRP IN PROGNOSTICATION OF PATIENTS DIAGNOSED OF HODGKIN'S LYMPHOMA: A PROSPECTIVE COHORT STUDY

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ABSTRACT Hodgkin's lymphoma (HL) constitutes around 30% of all lymphomas(1). IPS is used for the risk stratification of advanced stage HL but it lack applicability to the early stage cases(1)..In this prospective cohort study, we aim to confirm the relationship between hsCRP levels with treatment response (interim as well as end of treatment) of HL treated with the standard chemotherapy and radiotherapy regimens. A total of 50 patients were recruited over a period of 18 months and the patients were followed up in the hematology clinic and interim treatment responses as well as end of treatment response were assessed. Correlation of the hsCRP levels and the treatment response showed that the low levels of hsCRP level were associated with more advanced stages.. Univariate analysis showed that there was no significant correlation of interim treatment response as well as end of treatment response with hsCRP levels .

KEYWORDS :

INTRODUCTION

Classical HL represent nearly 95% of all the cases of HL–(2).A cure can be achieved in approximately 80% of the patients with current treatment regimen consisting of multi agent chemotherapy and radiotherapy (in selected cases).The remaining 20% attaining remission(4).Early identification of the patients who would fail treatment or relapse in future is currently a challenge. At present the most commonly used tool for prognostication of HL cases is international prognostic score(IPS) (on a scale of 0 -7), with higher scores indicating poorer prognosis)–(5).This score is a combination of clinical and basic haematological parameters recorded at the time of diagnosis of a case like age , gender ,stage, haemoglobin level ,albumin level and lymphocyte counts (1). Children and adolescents with classical Hodgkin's Lymphoma (HL) have an excellent prognosis . For these patients the prognostic role of stage IV, extranodal involvement, presence of B-symptoms, bulky disease, number of involved lymph nodes and elevated Erythrocyte sedimentation rate (ESR) was demonstrated by several studies. C-reactive protein (CRP) is produced by the liver and other organs in response to release of interleukin-6 by monocytes and other immune cells following infection and other conditions associated with tissue injury and inflammation(6) . Elevated levels of this marker of infection have been associated with increased risk of cardiovascular disease, as well as of increased overall mortality in the elderly(5) . A few studies have been recently published on the association between prediagnostic CRP level and cancer risk, which suggest in particular an increased risk of cancers of colorectum and ovary. Surprisingly CRP, which is induced by IL-6 and which is routinely determined as marker for inflammation in many diseases, has only been analyzed in very few reports dealing with HL patients – two reports investigated the role of CRP in children and three in adults(5). These studies consistently showed that elevated CRP levels correlate with the classical risk factors and/ or adverse outcome. However, two studies in adults with HL were published in the early 1980 with less intensive treatment and thus inferior outcome results than today. The more recent pediatric and adult studies, however, included only a small number of patients. In this study we aim to study the role of hsCRP levels to prognosticate the patient of Hodgkin's lymphoma .

MATERIAL AND METHODS

STUDY DESIGN

This was a prospective cohort study carried out in the patients diagnosed with Hodgkin's lymphoma who completed treatment at PGIMER, Chandigarh. Patients were enrolled in the study from the Adult Haematology Clinic PGIMER, Chandigarh prospectively from July 2017 to March 2018 and then they were followed up till November 2018.

DURATION OFTHE STUDY

July2017 – December. 2018

PLACE OF THE STUDY:

1. Department of Internal Medicine Adult Clinical Haematology Unit PGIMER,Chandigarh
2. Department of Histopathology, PGIMER, Chandigarh

INCLUSION CRITERIA

1. Primary diagnosis of Hodgkin's lymphoma confirmed by a tissue biopsy
2. Adequate lymph node tissue in the paraffin block
3. Treatment naïve patients

EXCLUSION CRITERIA

1. Patient previously treated with chemo radiotherapy before coming to PGIMER,. Chandigarh.
2. Patients who did not complete chemotherapy or end of treatment chemotherapy response assessment were excluded from further analysis.

METHODOLOGY

PROCEDURE

1. Demographic and disease data were recorded in a predesigned performa (annexure 3) and investigations were recorded as per the performa.
2. Collection of the clinical and the laboratory data of the newly enrolled cases was done in the study performa.
3. Biopsy numbers of the lymph node were taken from the Adult Haematology Clinic case record files and the paraffin block were retrieved from the archive of the Department of Histopathology.
4. Cases with adequate tissue in the paraffin block in the archives of the Department of Histopathology were selected and immunohistochemistry staining was performed.
5. hsCRP levels were done before starting the treatment of the patients fulfilling the inclusion criteria.
6. Correlation of hsCRP levels , and treatment response (interim as well as end of treatment response was assessed.
7. The interim treatment response was assessed with the PET CT SCAN after two cycles of the chemotherapy and the response was assessed by the Deauville criteria.
8. The end of treatment response was assessed with the

PETSCAN after completion of chemotherapy and the response was assessed by Deauville criteria.

STATISTICAL ANALYSIS

The descriptive statistics were used to study the response rates, Correlation was assessed between hsCRP levels and the response rate by using Chi square test. .Differences were considered as significant if the computed p value was less than theoretical p value i.e. 0.05. Univariate analysis was performed to assess the association between the hsCRP levels with the treatment response with SPSS, version 22.0.

RESULTS

During the study period, we recruited 60 consecutive, treatment naive patients of Hodgkin's lymphoma. Out of this cohort, there were few exclusions as following:

A. Three patients died before starting treatment.
B. Seven patients lost to follow up before completion of therapy.

Hence, their response ~to chemotherapy was not available (due to leaving the treatment before completion). Therefore, in the end, total 50 patients were selected. The patients were followed up in the hematology clinic and interim treatment responses as well as end of treatment response were assessed.

HsCRP LEVELS:

_Hs-CRP levels were measured in the cases under the study with the cut off values of 10mg/L, it was found that 59 percent of the cases had Hs-CRP levels cut off greater than 10 mg/L while 40.4% cases had levels of less than 10mg/L. Higher Hs-CRP levels were observed in advanced stages of the disease (stage 3-4). Also, there was no significant (p value 0.29) between HsCRP levels in the early and the advanced stages of disease.

ANALYSIS:

INTERIM TREATMENT RESPONSE:

Univariate analysis showed that total of 48 patients 19(39.5%) had hsCRP levels <10 and 29(60.4%) had hsCRP levels >10 ,similarly a total of 4 patients not in complete remission 2(50%) had hsCRP levels <10 and 2(50%) had hsCRP levels >10 Also,there was no significant correlation of interim treatment response with hsCRP levels as shown in table no 1..

END OF TREATMENT RESPONSE:

Univariate analysis showed that total of 48 patients in complete remission 25(52%) had hsCRP levels <10 and 23(48%) had hsCRP levels >10, similarly a total of 4 patients not in complete remission 3(75%) had hsCRP levels <10 and 1 patient (25%) had hsCRP levels >10.Also,there was no significant correlation of end of treatment response with hsCRP levels as shown in table no 2.

DISCUSSION

In this study, which is the prospective investigation carried out over a period of 18 months based on data available , we observed no association between circulating hsCRP concentration and overall risk of Hodgkin's lymphoma . In the study performed by Wieland et al. 95 pediatric patients with HL were treated at 2 hospitals over a 10 year period. The authors described a 100 % rate of relapse free survival in patients with CRP levels < 5 mg/l at diagnosis. All patients with relapse had elevated CRP levels at time of relapse, suggesting that CRP might be a parameter for treatment failure(3). In contrast, Bien et al. analyzed the prognostic role of CRP and ESR in 30 polish children and adolescents with HL and found no significant association between pre-treatment CRP and outcome (3) . This was probably due to the small patient sample. Axdorph et al.[1] found a significant association of elevated CRP and cause specifi c survival (CSS, defi ned as death, relapse or secondary malignancy) in 99 adults with HL. However, the CSS at 5 years was 82%.Previous study has reported that progression-free survival and overall survival of HL patients were negatively correlated with basal serum Hs-CRP levels "(23). In present study, we found no significant correlation of HsCRP levels with early and advance stages of disease. This could be again due to small sample size of our study.In the present study, we intended to correlate hsCRP levels with treatment response and survival outcomes but due to short follow up period of our study with only 4 relapses and no mortality, the effective number of events were very less. Hence we limited our study end point to treatment response only. Although present study put forward some evidence which bridge the gap of existing knowledge about role of M1 and M2 tumor related macrophages phenotype in treatment response in patients with HL, there still exist some limitation in present study.

CONCLUSION

In conclusion, HsCRP levels and low levels of vitaminD_3 were associated with advanced stages.There was no significant correlation between hsCRP levels with the treatment response interim as well as end of treatment response.

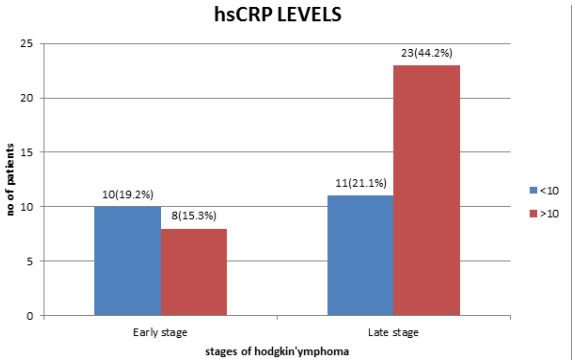

Figure.1.Hs-CRP levels in the various stages of the disease

CHARACTERISTICS OF PATIENTS WITH INTERIM TREATMENT RESPONSE

Table no 1. univariate analysis of Interim treatment response with various prognostic variables shows no significant correlation (p value <0.05)

Features	Number of patients in complete remission N (%)	Number of patients not in complete remission N (%)	P value
hsCRP levels			
<10	19(39.5%)	2(50%)	0.683
>10	29(60.4%)	2(50%)	

CHARACTERISTICS OF PATIENTS WITH END OF TREATMENT RESPONSE

Table no 2. univariate analysis of end of treatment response with various prognostic variables

Features	Number of patients in complete remission N(%)	Number of patients not in complete remission N(%)	P value
hsCRP levels			
<10	19(39.5%)	2(50%)	0.683
>10	29(60.4%)	2(50%)	

REFERENCES

1. Rugbjerg K, Maraldo M, Aznar MC, Cutter DJ, Darby SC, Specht L, et al. Long-term hospitalisation rates among 5-year survivors of Hodgkin lymphoma in adolescence or young adulthood: A nationwide cohort study. International journal of cancer. 2017;140(10):2232-45.
2. Ph D, Chan WC, Gascoyne RD. NIH Public Access. 2010;362(10):875–85.
3. Evaluation of the prognostic of C-reactive protein in children and adolescent with classical hodgkin's lymphoma Haase et al

4. Vardhana S, Younes A. The immune microenvironment in Hodgkin lymphoma: T cells, B cells, and immune checkpoints. Haematologica. 2016;101(7):794-802.
5. Plasma C-reactive protein and risk of cancer:A prospective study fron greece Dimitrios Trichopoulos, Theodora Psaltopoulou, Philippos Orfanos, et alCancer Epidemiol Biomarkers Prev2006;15:381-384
6. C-Reactive Protein Serum Level is a Valuable and Simple Prognostic Marker in Non Hodgkin's LymphomaE. legouffe", c. rodriguez', m.c. picot', b. richardd, b kleina, j.f. rossa and t. commesb