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RESEARCH ARTICLE

SERUM HIGH SENSITIVITY C-REACTIVE PROTEIN AS A PROGNOSTIC AND THERAPEUTIC MARKER IN ADVANCED STAGE NON-SMALL CELL LUNG CANCER

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ABSTRACT

Introduction: CRP is shown to be elevated in many malignancies including lung cancer. In patients of NSCLC, elevated CRP levels prior to therapy are related with bad prognosis. Studies have shown that high CRP is also related to advanced stages. CRP level is much higher in malignancy cases than only inflammatory condition like COPD. In cancer, CRP is possibly increased by tissue inflammation and cytokines released by tumor cells indicating a higher tumor burden.

Objective: This study was designed to evaluate serum mean hs-CRP levels in advanced stage NSCLC at diagnosis, after every 2 cycles of chemotherapy and to correlate this with treatment response. Baseline hs-CRP with correlated with tumor stage and T size and also compared with baseline levels in patients of COPD and healthy controls.

Material and Methods: This Hospital based observational study included 20 newly diagnosed patients of NSCLC (stage IIIB and IV) in good PS, 20 patients of stable COPD and 20 healthy controls. Baseline hs-CRP values were compared among three groups. NSCLC cases were assessed for baseline hs-CRP, tumor size, subtypes, staging and treatment response. After every 2 cycles of chemotherapy, parameters were reassessed and compared. hs-CRP was tested by routine clinical lab test protocols using instrument Labmate and tumor response was assessed using the RECIST 1.1 criteria.

Results: Baseline mean hs-CRP values of NSCLC, COPD, controls were 28.11±16.02 mg/L, 8.59±3.53 mg/L,0.60±0.30 mg/L respectively ($p<0.001$). Squamous Cell Carcinoma (SCC) had significantly higher CRP as compared to adenocarcinoma, and NSCLC-NOS. No statistical significance was found between SCC and large cell ca. After treatment, 15% had CR, 35% had PR, 25% had SD and 25% had PD. Baseline mean hs-CRP values in patients with CR, PR, SD and PD groups were 8.13±.80 mg/L,19.27±2.99 mg/L,29.60±6.2 mg/L and 50.98±8.6 mg/L ($p<0.001$).This statistical significant difference was also noted post 2nd, 4th & 6th cycle of chemotherapy. Significant difference was noted in baseline mean tumor size and mean baseline hs-CRP (cut off 7cm). Strong correlation was found in change in mean tumor size and mean hs-CRP during treatment in all treatment response groups($r > 0.8$).

Conclusion: Despite the small number of patients in our study, we conclude the following. A high CRP value could suggest an occult lung cancer in patients of COPD. Higher stages at diagnosis have high level of CRP. Patients with high baseline tumor size have high level of baseline CRP. During treatment change in hs-CRP and change in tumor size have strong correlation. Patients having high baseline hs-CRP level are less likely to respond to chemotherapy and have progressive disease. hs-CRP might be useful for monitoring treatment response in Ca lung.

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INTRODUCTION

C-reactive protein was discovered in 1930 and is widely used as a sensitive, but nonspecific, marker of systemic inflammation (Pepys *et al.,* 2013). CRP is an acute-phase protein, which can increase up to 1000-fold after the onset of a stimulus. Increased serum CRP levels have been reported in many pulmonary disorders, including pneumonia, malignancies, and pulmonary thromboembolism (Smith *et al.,* 1995).

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A high–sensitivity CRP (hs-CRP) test measures low level of CRP down to. 04 mg/L. Elevated levels of CRP are associated with an increased risk of all-cancer particularly lung cancer, and possibly breast, prostate, renal, melanoma and colorectal cancer (Guo *et al.,* 2013). It is positively correlated with weight loss, anorexia-cachexia syndrome, extent of disease, and recurrence in advanced cancer (Mahmoud and Rivera, 2002). The reasons for CRP elevation in cancer patients are not clearly understood, several possible mechanisms have been proposed for the relationship between CRP and cancer (Heikkilä *et al.,* 2007). One possible mechanism is that tumor cells themselves cause tissue inflammation and thus increase CRP levels.

Other possible explanation is that, due to cytokine production(IL-6) by tumor tissue, elevated CRP values may indicate a higher tumor burden. Another reason may be infection in cancer patients. In patients with Non-small cell lung cancer (NSCLC), elevated CRP levels prior to therapy have been shown to have an adverse impact on prognosis (Minseon *et al.,* 2012). It has been proven in many studies that High levels of CRP is related with higher stages and hence with poor prognosis. It is also observed in many studies that the CRP level is much higher in malignancy cases than only inflammatory condition like chronic obstructive pulmonary disease. A lot of literature has been published, supporting that increased CRP level is associated with chronic inflammation in various cancers and chronic inflammatory conditions like COPD. The study "Comparison of C-reactive protein levels in patients with lung cancer and chronic obstructive pulmonary disease" done by Vagulienė in et al established correlation of CRP levels in serum of patients with lung cancer and COPD.CRP levels were significantly higher in the lung cancer patients with or without COPD compared with the COPD patients or the control group. The patients with advanced lung cancer had higher CRP levels compared with the patients suffering from early stage lung cancer. The CRP levels were significantly higher in the patients with early stage lung cancer compared with the COPD patients. Chronic inflammation plays an important role in both diseases, lung cancer and COPD but it seems that inflammation is more pronounced in patients with lung cancer. In one study "CRP evaluation in NSCLC" published in Egyptian journal of Chest Diseases and Tuberculosis 2014 done by Hassan Aref et al, it was observed that elevated CRP was correlated with the advanced stages and increased tumor size in NSCLC.CRP level was significantly higher in patients with NSCLC compared to the control group There was a positive correlation between CRP level with tumor size & TNM tumor staging. This study was designed to evaluate serum mean hs-CRP levels in advanced stage NSCLC at diagnosis, after every 2 cycles of chemotherapy and to correlate this with treatment response. Baseline hs-CRP with correlated with tumor stage and tumor size and also compared with baseline levels in patients of COPD and healthy controls. hs-CRP level is associated with tumour size and staging of NSCLC cases and has prognostic and therapeutic value regarding management of disease.

MATERIALS AND METHODS

This is a hospital based comparative observational analytic study done over period of 24 months. We included 60 patients in our study. Diagnosis was made either by bronchoscopic biopsies in accessible lesions, transthoracic needle biopsy in peripheral lesions, pleural fluid aspiration in cases of concomitant malignant pleural effusion, excisional lung biopsies in cases not accessible by bronchoscopy or transthoracic route, transbronchial needle aspiration from subcarinal lymph nodes was done for the diagnosis and staging. After full investigation the TNM classification of each patient was recorded and serum hs-CRP was analyzed together with serum procalciton. We studied 3 groups including 20 patients in each group. Group-1 consisted of newly diagnosed patients of Non-Small Cell Lung Cancer stage IIIB and IV (PS 0/1/2), group-2 consisted of age & sex matched patients with chronic obstructive pulmonary disease (COPD) cases without exacerbation and group-3 consisted of age & sex matched healthy individuals as control cases. Patients were selected from patients attending medical OPD and R.K. Birla Cancer Centre OPD and medical in-patient wards. We measured mean hs-CRP levels after every two cycles of combination chemotherapy (three weekly) and correlated its level with response in NSCLC cases.

Selection of patients was done based on the following inclusion and exclusion criteria:-

Inclusion Criteria

- Newly diagnosed patients of advanced stage Non-Small Cell Lung Cancer (stage IIIB and IV) who are not candidates for surgery and/or radiotherapy of both sex in good PS: ECOG (PS 0/1/2) and with normal CBC, RFT & LFT (Minseon *et al.,* 2012).
- COPD cases without exacerbation and
- Healthy individuals having normal serum hs-CRP levels.

EXCLUSION CRITERIA

- Patients of NSCLC of both sex who have received CT/RT or Surgery for their disease.
- Patients in poor PS ¾
- Patients unwilling to give informed consent.
- Patients diagnosed as Small cell lung cancer.
- Patients under Radiation therapy.
- Any history of recent intake of systemic steroids or anti-inflammatory drugs.
- Presence of any other active inflammatory disease.
- Patients with severe systemic disease, hepatic or renal disease or uncontrolled infection.
- Pregnant females.

Following tests were done in all the selected patients

CBC/DLC/ serum biochemistry, hs-CRP level after every 2 cycle of chemotherapy. Chest CT scan before starting the chemotherapy and a repeat chest CT after every 2 cycles of chemotherapy, Maximum tumor diameter by CT scan chest baseline and after every 2 cycle, serum procalcitonin levels.

Statistical Analysis: Statistical analysis was performed with the SPSS, version 20 for Windows statistical software package. The Categorical data were presented as numbers (percent) and were compared among groups using Chi square test. While comparing Groups, data were presented as mean and standard deviation and were compared using by students t-test (for two Group) and ANOVA Test (more than two) and post Hoc test, applying to find out the most significant groups among all the groups. Repeated measure ANOVA was used for follow up quantitative variables. Probability P value <0.05 was considered statistically significant.

RESULTS

In each group 3(15%) cases were females and 17(85%) case were males. Values for mean age in 3 groups were 65.45+/-8.2(control group), 65.05+/-7.7(COPD cases), and 67.95+/-7.3 (NSCLC cases) in years. We found histologically 45% cases of squamous cell carcinoma, 30% adenocarcinoma, 15% large cell carcinoma and 10% others classified as Non- small cell carcinoma not otherwise specified (NSCLC-NOS). There were 12 cases in TNM stage IIIB and 8 cases in stage IV at the time of diagnosis.

Response group		HSCRP Baseline	After 2 cycles of chemo	After 4 cycles of chemo	After 6 cycles of chemo
CR	N	3	3	3	3
	Mean	8.13	6.50	2.43	.90
	Std. Deviation	.808	.700	.503	.100
PR	N	7	7	7	7
	Mean	19.27	14.84	12.13	9.23
	Std. Deviation	2.994	3.394	2.743	1.628
SD	N	5	5	5	5
	Mean	29.60	25.10	21.28	16.96
	Std. Deviation	6.260	3.013	2.765	5.271
PD	N	5	5	5	5
	Mean	50.98	58.90	64.28	71.58
	Std. Deviation	8.643	4.159	3.802	3.276
		<0.001S	<0.001S	<0.001S	<0.001S

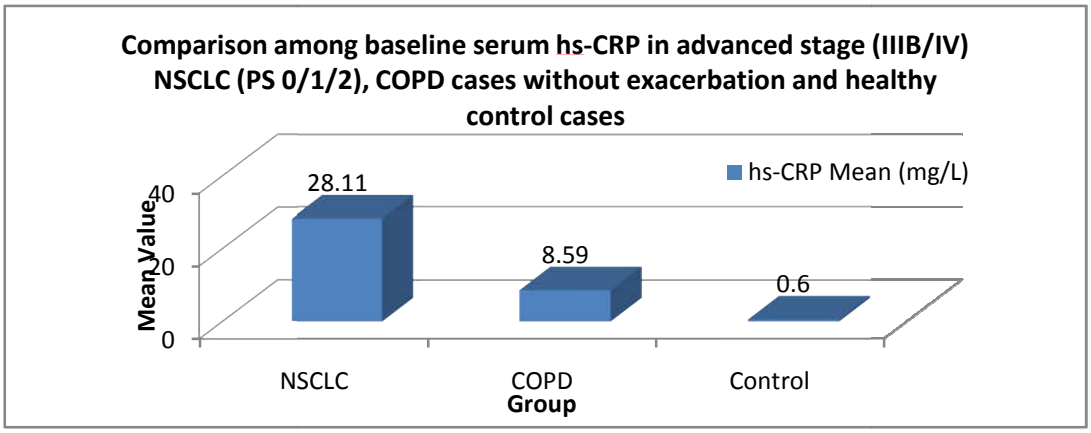

Fig. 1. Trend of change in value of hs-CRP during course of treatment and comparison among CR/PR/SD & PD groups in NSCLC cases during and after treatment

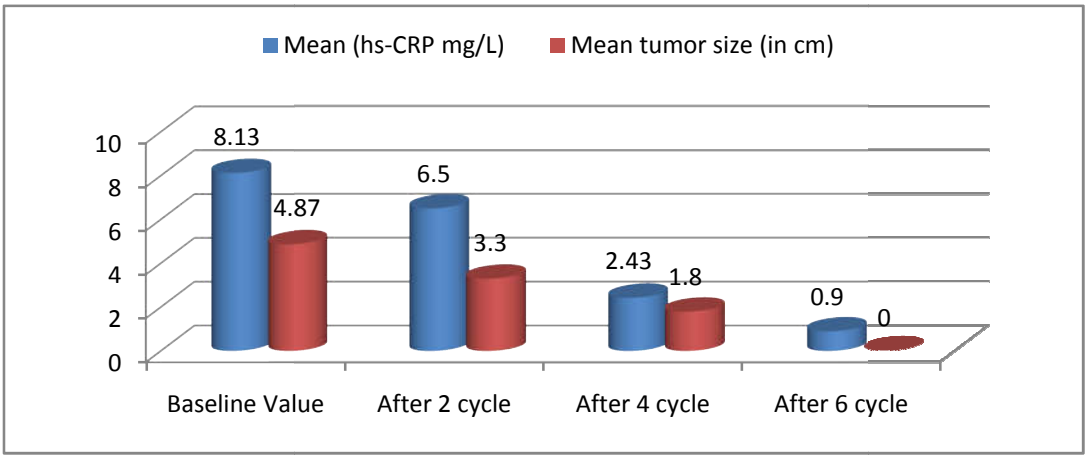

Fig.2. Correlation between mean tumor size and mean hs-CRP in patients having CR as final outcome

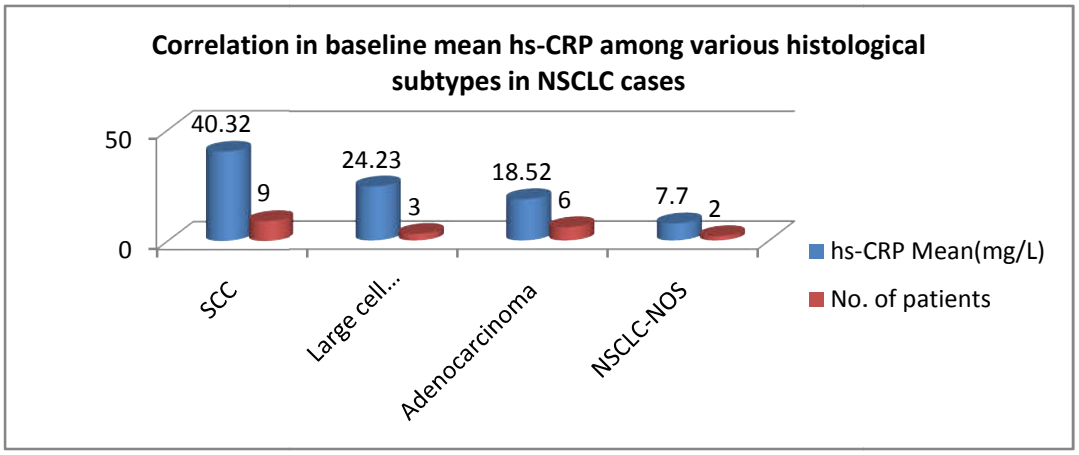

Fig. 3. Correlation in baseline mean hs-CRP among various histological subtypes in NSCLC cases

Cut off value for comparison of maximum tumor diameter (detected by CT scan) was taken 7cm and 17 cases(85%) had maximum tumor diameter more than 7cm and 3 case (15%) had size below 7 cm. The results regarding baseline characteristics (complete blood counts, liver function tests and renal function tests) among three group were within normal reference limits. In NSCLC group (20 patients), 6 cycles of combination chemotherapy (paclitaxel + carboplatin) were transfused, every 3 weekly. Serum mean hs-CRP values of NSCLC, COPD and Normal healthy controls cases were found 28.11±16.02 mg/L ,8.59±3.53 and 0.60±0.30 mg/L respectively. In stage IIIB group and IV group baseline mean hs-CRP values were noted 17.35±6.32 mg/L and 44.25±11.75 mg/L respectively. Squamous Cell Carcinoma cases have significantly higher baseline mean hs-CRP values as compared to adenocarcinoma, and NSCLC-NOS cases having hs-CRP values 40.32±16.08 mg/L,18.52±2.44 mg/L,7.7±0.424 mg/L respectively.

Out of 20, 12 patient were in stage IIIB and 8 in stage IV, at the time of diagnosis. In stage IIIB group and IV group baseline mean hs-CRP values were noted 17.35±6.32 mg/L and 44.25±11.75 mg/L respectively. Squamous Cell Carcinoma, adenocarcinoma, and NSCLC-NOS cases had hs-CRP values 40.32±16.08 mg/L vs 18.52±2.44 mg/L vs7.7±0.424 mg/L respectively.17 patients with tumor size more than 7cm had mean hs-CRP of 30.82±19.47 mg/L and 3 patients who had tumor size of less than 7 cm and had mean hs-CRP 6.5±0.7 mg/L. After completion of chemotherapy we found treatment response applying RECIST1.1 criteria. Out of 20, 3 patients (15%) progressed to complete remission (CR), 7 patients (35%) progressed to partial remission (PR), 5 patients (25%) showed stable disease (SD), 5 patients (25%) did not show any improvement and labeled as progressive disease group (PD).We observed mean serum hs-CRP levels after every two cycle of chemotherapy in all four treatment response groups(CR,PR,SD and PD) and compared them with each other statistically. Baseline mean hs-CRP values in CR, PR ,SD and PD groups were 8.13±.80 mg/L,19.27±2.99 mg/L, 29.60±6.2 mg/L and 50.98±8.6 mg/L. After 2ndcycle, mean hs-CRP values in CR, PR,SD and PD groups were 6.5±0.7 mg/L,14.84±3.39 mg/L, 25.10±3.01 mg/L and 58.90±4.1 mg/L respectively. After 4th cycle, mean hs-CRP values in CR, PR,SD and PD groups were 2.4±0.5 mg/L,12.13±2.74 mg/L, 21.28±2.76 mg/L and 64.28±3.8 mg/L respectively. Finally, After 6th cycle mean hs-CRP values in CR, PR,SD and PD groups were 0.9±0.1 mg/L,9.23±1.62 mg/L, 16.69±5.2 mg/L and 71.58±3.27 mg/L.
In CR group, during the course of treatment, correlation was observed between change in mean tumor size and change in mean serum hs-CRP value. Mean hs-CRP from baseline value 8.13±0.808 mg/L changed to 6.5±0.7 mg/L after 2nd cycle, 2.43±0.503 mg/L after 4th cycle, 0.9±0.1mg/L after 6th cycle. It was compared with change in mean tumor size from baseline value 4.87±0.8 cm that changed to 3.3±0.3 cm after 2nd cycle, 1.8±0.26 cm after 4th cycle, not detectable after 6th cycle. Residual tumor was considered as size zero for statistical analysis (negligible).In PR group, we also correlated change in mean tumor size and change in mean serum hs-CRP value. Mean hs-CRP from baseline value 19.27± 2.94 mg/L changed to 14.84±3.39 mg/L after 2nd cycle, 12.13±2.74 mg/L after 4th cycle, 9.23±16.28 mg/L after 6th cycle. It was compared with change in mean tumor size from baseline value 8.44±1.06 cm that changed to 7.23±1.17cm after 2nd cycle, 6.38±0.84 cm after 4th cycle, 5.56±0.58 cm after 6th cycle. In SD group, mean hs-CRP from baseline value 29.60±6.2 mg/L changed to 25.10±3.01 mg/L after 2nd cycle, 21.28±2.76 mg/L after 4th cycle, 16.96±5.27 mg/L after 6th cycle. It was compared with change in mean tumor size from baseline value 11.54±1.02 cm that changed to 10.64±0.89 cm after 2nd cycle, 9.50±0.97 cm after 4th cycle, 8.62±0.950 cm after 6th cycle. In PD group, mean hs-CRP from baseline value 50.98 ±8.64mg/L changed to 58.90±4.159 mg/L after 2nd cycle, 64.28±3.802 mg/L after 4th cycle, 71.58±3.276mg/L after 6th cycle. It was compared with mean tumor size from baseline value 13.30±0.48cm that changed to 13.98±0.33cm after 2nd cycle, 14.9 ±0.65 cm after 4th cycle, 16.16±0.55 cm after 6th cycle.

DISCUSSION

In this study there was statistically no difference regarding sex ratio and age among three groups. When we compared baseline serum hs-CRP in all 3 groups, we found that significant difference was noted among all three groups. hs-CRP values of NSCLC, COPD & controls cases were found 28.11±16.02 mg/L, 8.59±3.53 mg/L ,0.60±0.30 mg/L respectively. COPD patients have statistically significant high values of hs-CRP than control group cases. In terms of clinical implication, this finding could indicate that patient of COPD who show a high level of hs-CRP should be aggressively investigated to rule out the co-existence of lung cancer. These results were similar to a study“ Comparison of CRP levels in patients with lung cancer and COPD” done by Vagulienė et al. Another important finding of this study was that the baseline mean hs-CRP values in patients with CR, PR ,SD and PD groups were 8.13±.80 mg/L,19.27±2.99 mg/L, 29.60±6.2 mg/L and 50.98±8.6 mg/L respectively showing significant difference (P value<.001) among these groups. After 2nd cycle, mean hs-CRP values in patients of CR,PR ,SD and PD groups were 6.5±0.7 mg/L,14.84±3.39 mg/L, 25.10±3.01 mg/L and 58.90±4.1 mg/L respectively showing statistical significant difference (P value<.001) among these groups. After 4th cycle, mean hs-CRP values in patients of CR,PR ,SD and PD groups were 2.4±0.5 mg/L,12.13±2.74 mg/L, 21.28±2.76 mg/L and 64.28±3.8 mg/L respectively showing again significant difference (P value<.001) among these groups. Finally, After 6th cycle mean hs-CRP values in patients of CR,PR ,SD and PD groups were 0.9±0.1 mg/L,9.23±1.62 mg/L, 16.69±5.2 mg/L and 71.58±3.27 mg/L respectively showing significant difference (P value<.001) among these groups. We found significant difference at each comparison point (post 2nd, 4th& 6th cycle of chemo) among patients of all 4 groups.

This indicate that patients who have a higher baseline hs-CRP level are less likely to response to chemotherapy and more likely to have progressive disease. This could be a useful prognostic marker. One more observation of this study was the correlation between hs-CRP level and tumor stage. In stage IIIB group and IV group mean hs-CRP values were noted 17.35±6.32 mg/L and 44.25±11.75 mg/L respectively. We observed significant difference in mean hs-CRP between these 2 groups. Similar results were found in study done by Hassan Aref and Sherif refaat. There was a statistically significant higher level of CRP associated with advanced stages of NSCLC. Magnitude of hs-CRP at baseline could be marker of tumor load. hs-CRP level was correlated with tumour size and we observed that baseline values of mean tumor size at time of diagnosis is significantly associated with mean hs-CRP level in patients of NSCLC. 17 patients (85%) had tumor size > 7cm and mean hs-CRP of these patients was 30.82±19.47 mg/L.
It was compared with 3(15%) patients who had tumor size of < 7 cm and had mean hs-CRP 6.5±0.7 mg/L. We observed

significant difference between these two groups. These results are comparable to study done by Hassan Aref and Sherif refaat. This was also matching with a study done by Lee et al "Preoperative CRP levels associated with tumor size and lymph vascular invasion in resected NSCLC". In a study "Serum CRP and procalcitonin levels in NSCLC patients" done by Baykal Tuleket alalso established same correlation.

In CR group, during the course of treatment, correlation was observed between change in mean tumor size and change in mean serum hs-CRP value. hs-CRP from baseline value 8.13±0.808 mg/L changed to 6.5±0.7 mg/L after 2nd cycle, 2.43±0.503 mg/L after 4th cycle, 0.9±0.1mg/L after 6th cycle. It was compared with change in mean tumor size from baseline value 4.87±0.8 cm that changed to 3.3±0.3 cm after 2nd cycle, 1.8±0.26 cm after 4th cycle, not detectable after 6th cycle. We found strong correlation between these two variables with R values > 0.8 at different four comparison points. Similarly in PR group, correlation was observed between change in mean tumor size and change in mean serum hs-CRP value. Mean hs-CRP from baseline value 19.27± 2.94 mg/L changed to 14.84±3.39 mg/L after 2nd cycle, 12.13±2.74 mg/L after 4th cycle, 9.23±16.28 mg/L after 6th cycle. It was compared with change in mean tumor size from baseline value 8.44±1.06 cm that changed to 7.23±1.17cm after 2nd cycle, 6.38±0.84 cm after 4th cycle, 5.56±0.58 cm after 6th cycle. We found strong correlation between these two variables with R values > 0. 8 at different four comparison points, as described above.

In SD group, correlation was observed between change in mean tumor size and change in mean serum hs-CRP value (shown in table no.18). Mean hs-CRP from baseline value 29.60±6.2 mg/L changed to 25.10±3.01 mg/L after 2nd cycle, 21.28±2.76 mg/L after 4th cycle, 16.96±5.27 mg/L after 6th cycle. It was compared with change in mean tumor size from baseline value 11.54±1.02 cm that changed to 10.64±0.89 cm after 2nd cycle, 9.50±0.97 cm after 4th cycle, 8.62±0.950 cm after 6th cycle. We found fair to strong correlation between these two variables with R values (0.3 to >0.8) at different four comparison points. Lastly in PD group, correlation was observed between change in mean tumor size and change in mean serum hs-CRP value. Mean hs-CRP from baseline value 50.98 ±8.64mg/L changed to 58.90±4.159 mg/L after 2nd cycle, 64.28±3.802 mg/L after 4th cycle, 71.58±3.276mg/L after 6th cycle. It was compared with mean tumor size from baseline value 13.30±0.48cm that changed to 13.98±0.33cm after 2nd cycle, 14.9 ±0.65 cm after 4th cycle, 16.16±0.55 cm after 6th cycle. We found strong correlation between these two variables with R values > 0. 8 (strong correlation) at different four comparison points.

Our study also correlates difference in baseline mean hs-CRP among various histological subtypes

In study done by Hassan aref and sheriff refaat (Hassan Aref *et al.,* 2014), CRP level in different subtypes of non-small cell lung cancer (NSCLC) did not show statistical significant difference but in our study Squamous Cell Carcinoma cases have significantly higher baseline mean hs-CRP values as compared to adenocarcinoma, and NSCLC-NOS cases having hs-CRP values 40.32±16.08 mg/L,18.52±2.44 mg/L ,7.7±0.424 mg/L respectively although there was no statistical significance between SCC and large cell carcinoma (24.23±1.487 mg/L) subtype (p value >0.05). Our results are somewhat similar to study done by Lee et al in which serum CRP levels were significantly associated with histology (squamous >> non-squamous, $p = 0.001$) but he did not mention non squamous subtypes separately. During study we did not see significant difference in the baseline serum procalcitonin levels in these groups indicating that the rise of CRP in the patient group and COPD and healthy controls was not related to infectious aetiology(P value 0.823)..No significant difference was observed in serum procalcitonin levels in NSCLC cases during course of treatment comparing baseline, after 2nd, 4th, 6th cycles with P value 0.597. Serum procalcitonin is seen higher in patients with active bacterial infection and there is no available data in the literature to support rise of PCT in various cancer patients so it was used to exclude patients with lung cancer associated with infectious aetiology. We have a lot of published literature regarding role of hs-CRP in cancer patients.

A study titled as"Association between C-reactive protein and Cancer Risk, Mortality" showed that high levels of CRP is associated with the risk of developing cancer and with earlier cancer death.In a study "CRP and Risk of Lung Cancer" done by A chaturvedi (Hassan Arefet *et al.,* 2014), investigated association of circulating hs- CRP with prospective lung cancer risk.One another study"Circulating Inflammation Markers, Risk of Lung Cancer, and Utility for Risk Stratification" done by Meredith S. Shiels et a, observed that circulating inflammation markers like CRP reproducibly associated with lung cancer risk and it can be used for lung cancer risk stratification. A study "CRP Levels, Variation in the C - reactive protein Gene, and Cancer Risk: The Rotterdam Study" examined whether CRP levels and *CRP* gene variations were associated with an altered risk of colorectal, lung, breast, or prostate cancer. One study "The role of C-reactive protein as a prognostic indicator in advanced cancer" concluded that increased CRP level is positively correlated with weight loss, anorexia cachexia syndrome, extent of disease, and recurrence in advanced cancer. Its role as a predictor of survival has been shown in lung, multiple myeloma, melanoma, lymphoma, ovarian, renal, prostate, pancreatic, and gastrointestinal tumors.

A study "Elevated Serum CRP as a Prognostic Marker in Small Cell Lung Cancer" investigated CRP as a prognostic marker in small cell lung cancer. Median overall survival in the normal CR*P* grou*p* was significantly longer than with the high CRP group.In a study "Elevated pre-treatment levels of plasma CRP are associated with poor prognosis after breast cancer"examined that plasma CRP levels at the time of diagnosis of breast cancer are associated with overall survival, disease-free survival, death from breast cancer, and recurrence of breast cancer. In ASCENT trial, by Beer et al.it was reported that, "Elevated plasma CRP concentrations appear to be a strong predictor of poor survival and lower probability of PSA response to treatment in patients with castration-resistant prostate cancer. High CRP values predict poor survival in patients with penile cancer. Sandra Steffens *et al.* 2010 showing significantly elevated CRP level was found more often in patients with an advanced tumor stage and in those with nodal disease at diagnosis. Study "Inflammation Marker Predicts Colon Cancer" by Thomas "Tate" et al showed that people with higher levels of CRP in their blood were more likely to develop colorectal cancers than those with low levels. Higher CRP is also associated with worse survival in patients with Melanoma. A study by Shenying Fang et al, showed that patients with CRP less than 10 mg/L, have better survival than >10mg/L. Study "Prognostic role of serum C-reactive protein in esophageal cancer" by Ying Huang et al, observed that a

high level of serum CRP was associated with poor Overall Survival. The elevated serum CRP is strongly related to risk of cancers especially lung cancer in recent meta-analysis studies. So hs-CRP can be used as a therapeutic marker to guide management of NSCLC cases regarding response of therapy and it's level are strongly correlated with tumor load and stage of cancer hence relates with prognosis of disease.

Conclusion

Patients of advanced stage NSCLC stage have high baseline serum hs-CRP than COPD and healthy controls and also COPD patients have high baseline hs-CRP as compared to healthy controls. We conclude that hs-CRP can be a valuable marker for response of treatment, showing its therapeutic utility. Higher stages have high level of CRP. hs-CRP level is correlated with tumour size. Patients who have high tumor size at time of diagnosis have high level of baseline CRP as compared to low tumor size showing its prognostic utility. Change in hs-CRP and change in tumor size have strong correlation, whatever the response of disease remain during treatment.

Thus CRP level can guide treatment response as guided by tumor size showing its therapeutic value. Squamous Cell Carcinoma cases have significantly higher baseline mean hs-CRP values as compared to adenocarcinoma, and NSCLC-NOS. SCC case also have high value than large cell variety but a statistical significance was not established in between these two varieties. There is available published literature signifying that hs-CRP can be used as an indicator for poor survival and poor prognosis, in prospective of lung cancer which is one of the most prevalent cancers in India, our study might prove to be a breakthrough study revolutionizing the treatment strategies in this subset of malignancies in the times to come. However, larger multi-center studies are still needed to confirm our findings and evaluate the role of hs-CRP in NSCLC cases.

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