ORIGINAL ARTICLE

Frequency of Chronic Hepatitis Viral Infections Association among Multiple Myeloma Patients

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ABSTRACT

Background: Malignancies of lymphoid system is treated with use of some steroids groups, as a consequence these agents leads to aggravate ch viral hepatitis. In multiple myeloma (MM) hepatitis infection occurrence is unclear.
Aim: To investigate the individuality & conclusion of MM subjects in the corporation of ch hepatitis viral infections.
Methods: For the fulfillment of all criteria's 150 MM subjects were selected and undergone laboratory examination to find out their status regarding viral infection for chronic hepatitis by means of viral serology tests for hepatitis B and hepatitis C (HBV, HCV) respectively.
Results: The predictable pervasiveness of chronic infections of hepatitis B and C were 20(26%) and 18(23.7%) correspondingly. Patients who have carrier and those have not had different characteristics. Cyto-genetic abnormalities index were high in subjects of carrier state (58.3% vs. 20.5%). Collective frequency of 3-4 grades increase in Alanine transaminase (ALT/SGPT) levels 21% vs. 12.5%, and Hyper-bilirubinemia 10.5% vs. 0.8%, were elevated as well in carrier subjects. According to research over all poor survival in carriers patients were recorded (median=15.0 vs. 40.1 months). The predictive worth of carriers category were not significant statistically in multiple studies, but age group >64.5 years, the existence of abnormalities in cytogenetic analysis, increase in beta-2-microglobulin intensity >3.3 mg/L, and the level of creatinine in serum > 1.9mg/dl were all include as self-regulating feature related with reduced prognosis.
Conclusion: Pattern of our study resolute the pervasiveness of HBV & HCV infection in MM diagnosed patients projected with the intention of these subjects may consist of a separate sub-group along with increased liver injuries and poorer rate of survival.
Keywords: Hyper-bilirubinemia, Alanine transaminase, Cyto-genetic abnormalities, 'Chronic Hepatitis B' viral

INTRODUCTION

Propagation of plasma cells from bone marrow leads to B-cell malignant cells (MM). In clinical observation it is evident that MM often associated with failure of kidney function, hypercalcemia, anemia, and bone abnormalities. Multiple chemotherapeutic drugs with steroids are the main stay of treatment in MM[1]. In previous years drug options have been increased for treatment of MM. The new innovative compounds increase the effectiveness and progress endurance. On the other hand steroids still count as most important constituent in these original treatments. Though, immune-suppression therapies like steroids and cytotoxic compounds causes unrestrained duplication of viruses of Hepatitis B and C, pursue by an embellished immunological reaction to hepatocytes infected with viruses, which than stimulate repeated activation or acutely exacerbate the hepatitis viral infections[2] Multiple research studies revealed that steroids used without other combinations can also had harmful consequence on hepatitis virus infected subjects. Occurrence of (HBV) in patients of lymphocytic cancers during receiving treatments in combination of cytotoxic compounds, and these can be life threatening sequel. According to previous studies subjects with blood malignancy associated with HBV positive stat, who have received chemotherapy they are more prone to have liver damage than those with only more prone to have liver damage than those with only carrier stat, this data analysis suggested that infection of (HBV) may impede with chemotherapy agents and influence the effects of patient. Multiple studies also inspect infections of HBV in B- cell line cancer subjects demonstrated in general carriers survival accompanied with hepatic impairment was drastically reduced as compare with subjects having normal liver function. In comparison with liver dysfunction and occurrence of HCV is not common between patients receiving chemotherapeutic agents for lymphoma or blood disorder. Still, patients with HCV positive has been counted as considerable threat for non-relapse able transience after receiving genetically incompatible stem cell transplant (SCT)[3]. In spite of plentiful studies explore the effect of hepatitis in lymphoid cell malignancies; preceding researches have integrated a reduced figure and results of MM subjects. Pakistan is prevalent area for HBV and HCV, with prevalence's of 6.1% and 20.3%, correspondingly. Non-Hodgkin's type of lymphoma has higher prevalence associated with HBV in early years have been reported around 22.3%, and HCV has same rate of occurrence as common inhabitants (3.9%). The mean of the existing research was to evaluate the frequency of hepatitis viral infections of chronic stage and to explore their distinctiveness and analytical implication in a following sequence of myeloma subjects[4].

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MATERIALS AND METHODS

Diagnosed and selected150 subjects of MM during research out of which 95 diagnosed patients around (63.5%) were register for research analysis. MM cases diagnosis were included on the basis of staging system used internationally. Diagnosed patients of mono-clonal gammopathy were not included in this study. Clinical and laboratory data variables were repossessed from the previously saved data in hospitals. Bone marrow samples analysis done by using techniques called Giemsa-banding staining. During using this method if at least two mitotic cells observed as having similar chromosomes or abnormality in there structure or loss of similar chromosomes a patient were believed to have abnormality in cytogenetic analysis.

Statistical analysis: The association among variables and subjects having hepatitis virus were assess by means of Fisher's exact test, as suitable. Record is maintained from day first from appearance of side effects regarding hepatic dysfunction following MM diagnosis. Two groups were made according to grades in which unfavorable events were compared by means of fisher test. The last end survival was calculated from first day of diagnosis till fatality. Cox comparative vulnerability form was used in uni and multi-variate analysis to conclude persuade of variables in overall survival rate. Variables around p< 0.10 of the uni-variates were incorporated with the multi-variate analysis. SPSS version 25.0 is used for data analyses.

RESULTS

Along with 150 diagnosed patients of MM, out of which 38 carrier patients of chronic hepatitis, and predictable frequency was 25.3%. Among these carriers, 17 were HBsAg positive (11%) 14 were anti-HCV positive (9%), and one patient was infected with HBV in addition to HCV concurrently. The overall median age of 150 subjects included in this study was around 68.0years age limitations between 30–90 years, in which 90 patients (58.0%) 67 years older. The follow-up was ranging between 0.3-80.9 months with median 20.6 months. As international staging system suggested (80/150) 53.3% were in stage 3 according to their classification. All the baseline variables and lab results are analogous in spite of carrier or non carrier position. Among the two groups the subject receiving chemotherapies or SCT were similar. Total data of cytogenetic aberration of 90 subjects was accessible, these abnormalities are all were multifarious karyotypes, details in 27.7% (25/90) of patients (Table 2). Atypical karyotypes were found 7/12 in carriers subjects, the significantly high frequency between carriers than non-carrier. (58.3% vs. 20.5%) with (P- value=0.003). Cytogenetic alterations were designated as high risk factors like hypo-diploidy, deletion of chromosome 13, and abnormalities of chromosome 11q abnormalities, 12-13 were initiate in 12(13.3%), 11(12.2%), and 4(4.4%) patients, correspondingly. Patients with carrier status having a considerable quantity of this unfavorable cytogenetic abnormality as well (16.6%, 16.6%, and 8.3%, respectively). Increased rate of liver injury and its incidence after chemotherapy in hematological cancers is found in patients having HBV positive status. To inspect the frequency of liver injury in carrier subjects with MM, alterations in the level of total bilirubin were observed during entire treatment plans. Out of the 20 HBV carriers patients 16 were received antiviral therapy as prophylactic treatment (tenofovir n=3) or (telbivudine n=13) 16/20 (80%). No anti viral therapy for HCV carrier patients. Higher frequency of raise in ALT and AST in carrier groups in 3-4 grades (21.0% vs. 12.5% P-value 0.014 and13.1% vs. 8.9% P-value=0.078 respectively. Increased in total bilirubin level more commonly recorded in 3-4 grades in carrier patients 10.5% vs. 0.8% P-value=<0.001.

Hyperbilirubinemia were increased continuously among preceding years. In spite of prophylaxis with telbivudine, patients having jaundiced and to converted into hepatitis B antigen sero-positive. The predictable possibility of overall survival (OS) between carriers were less than between non- carrier subjects 15.0 vs. 40.1 months OS. Out of 38 patients 12 patients died due to other causes except MM. (five from carriers and seven from non carrier groups). Eight out of these deaths were due to cardiovascular events, and four patients were died due to reactivation of HBV along with liver failure. In uni-variate analysis different feature predisposed OS rate including age, sex, ISS, cytogenetic abnormality, platelet count, b-2-microglobulin level serum calcium, albumin and creatinine. Age ≥65 years, the existence of cytogenetic abnormality, and creatinine level >2.2 mg/dl, p = 0.001 remains significant prognostic criteria during statistical analysis.

Table 1: Physical and laboratory characteristics of 150 MM patients according to viral hepatitis carrier status

Cyto-genetic transforms	**Non carriers (n=112)**	**Carrier (n=38)**	**P value**
Age ≥69 years	70(62.5%)	20(52.2%)	0.800
Male sex	8979.4%)	22(57.8%)	0.606
Serum M-protein			0.384v
IgG	63	13(34.2%)	
IgA	38	14(36.8%)	
Light chain disease	18	4(10.5%)	
Presence of plasmacytoma	5	3(7.8%)	0.494
Bone lesion(s)	16	5(13.1%)	0.644
ISS stage			0.805
1	34(30.3%)	13(34.2%)	
2	24(21.4%)	6(15.7%)	
3	64(57.1%)	20(52.6%)	
Baseline lab parameters			
Beta 2 m 3.5 mg/L	93(83%)	23(60.5%)	0.832
Albumin ,3.5 g/L	55(49.1%)	14(36.8%)	0.885
Hemoglobin ,10 g/dL	76(67.8%)	19(50%)	1.00
Platelets ,1006109/L	34(30.3%)	7(18.4%)	0.840
Serum calcium 12.0 mg/dL	12(10.7%)	6(15.7%)	0.204
Serum creatinine 2.0mg/dl	38(33.9%)	14(36.8%)	0.125
Serum ALT upper normal limit	17(15.1%)	5(13.1%)	0.950
Number of therapies			0.428
0-1	57(50.8%)	18(47.3%)	
2	34(30.3%)	6(15.7%)	
≥3	3531.2%)	9(23.6%)	
Use of thalidomide	68(60.7%)	12(31.5%)	0.068
Use of bortezomib	18(16%)	6(15.7%)	0.842
Stem cell trans-planttation	32(28.5%)	5(13.1%)	0.388

Table 2- Cytogenetic abnormalities detected in 90 MM patients.

Cyto-genetic transforms	(n=90)	Non carriers (n=78)	Carrier (n=12)
Normal	62 (68.8)	56 (71.7)	4(33.3)
Abnormal	25 (27.7)	16 (20.5)	7 (58.3)
Hypodiploidy	12 (13.3)	9 (11.5)	2(16.6)
Del (13)	11 (12.2)	8 (10.2)	2(16.6)
11q abnormalities	4(4.4)	2 (2.5)	1 (8.3)

Table 3- Frequency of liver injury in 150MM patients and overall survival in carriers vs. non carriers

	Non-carrier (n=112)	No: of carrier patients %			P value
		n=38	HBV (n=20)	HCV (n=18)	
ALT elevation (Grade 3-4)	14(12.5)	8(21.0)	4(20.0)	3(16.6)	0.014
AST elevation (Grade 3-4)	10(8.9)	5(13.1)	3(15.0)	2(11.1)	0.078
Hyperbilirubinemia (Grade 3-4)	1(0.8)	4(10.5)	3(15.0)	1(5.5)	<0.001
Viral hepatitis (carriers vs. non-carriers) OS					0.004

DISCUSSION

The outcome of this recent study discloses that the effects of HBV & HCV viral infection are significant in subjects of lymphoma as well as for MM patients. Carrier status was linked with cyto-genetic abnormalities, experiences additional hepatic injuries and poorer survival rate throughout the complete treatment ways[5]. The recent study has recommended that HBV and HCV infections have a pathogenic part in lymphoma as well as in multiple myeloma. Only some researches survey the relationship between multiple myeloma and HBV. Our research gives outcomes and discovered an elevated frequency of HCV infection in subjects of MM. Presence of cytogenetic abnormality in our study population is considered an exclusive characteristic in carrier group and used as powerful prognostic feature for poor overall survival rate. The genetically toxic effects of HBV & HCV lead to DNA disintegration of lymphocytes in peripheral blood. Chronic hepatitis status may act as contributor in the vulnerability of plasma cells, for the incurable discrimination of lymphocytes, to instable genetically and ensuing cyto-genetic abnormalities[6]. On the other hand MM associated with HBV or HCV subjects also develops early liver injury during course of treatment. Increase unfavorable proceedings throughout the treatment didn't clarify the differentiation in received therapies. To determine the carrier group it was mandatory to be in close-follow up regarding liver function test (LFT's) in prevalent areas. On the other hand, conservative cyto-genetic abnormalities preserve its prognostic importance in a quantity of situations. Due to low proliferation the MM cells are complicated for karyotyping as a result an abnormally higher karyotyping is useful indicator of poor prognosis. In our study, the existence of intricate karyotyping and a considerable section of patients with abnormalities may give details of undesirable results by means of abnormal cyto-genetic alterations. [7] Additional researches integrate with (FISH analysis) were essential to validate the alliance among hepatitis infection and cyto-genetic aberrations. For reactivation of HBV prevention for the period of chemotherapy, telbivudine is suggested to be used as prophylaxis in subjects of lymphoma with HBsAg +ve and in subjects with precedent HBV +ve infection. This approach in MM subjects even though for suggestions is not as clearer. In our study, nearly all of the prophylaxis for HBV +ve patients (15/17) was specified in perspective of subordinate prophylaxis. This fact may be endorsed to the partial compensation to prophylactic compounds in preceding times. For that reason, the contact of prophylaxis with anti-viral on the advancement of hepatic undesirable measures May not included or practical[8]. Prospective studies indicate that the prominent responsibilities of prophylaxis with anti-viral agents in MM patients in association with HBV infection are necessary[9,10]

CONCLUSION

Pattern of our study resolute the pervasiveness of HBV & HCV infection in MM diagnosed patients projected with the intention of these subjects may consist of a separate sub-group along with increased liver injuries and poorer rate of survival. Viral markers are diagnostic and are mandatory to recognize these patients, and on customary supervise for liver function should be compulsory. Prophylaxis with anti-viral agents plays a vital role in the management of patients infected with HBV, even though this prophylaxis may necessitate justification in successive researches.

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