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Research Article

Incidence of Multiple Myeloma in Iraqi People

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ABSTRACT

Multiple myeloma patients were carried out the period (October/2017-February/2018), for measurement the concentrations of IgM, IgM & IgG antibodies, types of light chains (kappa & Lambda) alpha-1,2 and gamma as well as albumin & protein levels in the sera of 47 (25 males & 22 females) patients compared with 29 healthy humans as control group. The diagnosis of patients were done by immunofixation technique.The positive titer of immunoglobulins showed 2(2.6%) IgM ,6(7.6%) IgA &33(43.4%) IgG, while 6(7.8%) was negative titer. The light chains Kappa 22(28.9%), Lambda 20(26.3%), while 5(6.6%) negative, it was noticeable changes among patients and healthy group. The alpha-1 in patients 19(25%), alpha-2 14(18.5%), beta 9 (11.8%), gamma 37(48.7%) were abnormal in patients of multiple myeloma (observed changes). Abnormal concentration of albumin and protein in the multiple myeloma patients showed 28(36.8%),18(23.6%) respectively also highly observed changes within patients and healthy group.

Keywords: Multiple myeloma, plasma cell, Immunofixation- electrophoresis.

INTRODUCTION

Multiple myeloma is created by plasma cells, the typical plasma cells are present in the bone marrow tissue and are an essential component of the immune defense, these cells make immunoglobulin's that aid the body hit and kill microbes, lymphatics are in several parts of the body: bone marrow, lymph nodules, intestine, blood stream, once B-lymphocytes became malignant and develop to abnormal cells, they generate a malignant known a" plasmacytoma", these cancerous cells increase in the bone while they are infrequently in other organs. If somebody shows just a single plasmocyte cancer, diverse is named an lonely "plasmacytoma", somebody exhibits extra than one plasmacytoma, they have multiple myeloma[1]. The immune response keep the creation of B cells and production of immunoglobulins under firm manage, when genetic materials are destructed, frequently through reorganization, this manage is misplaced, a advocate gene transfer to DNA, there it stimulate an immunoglobulin gene to over access, the chromosomal translocating among the heavy chain gene of antibody (on chro. 14, position 20911) is often noticed in multiple myeloma patients and this alteration resulting in irregulation of oncogenic cells that is attention to have central beginning happening in the immune mechanism of myeloma[2]. Cells of multiple myeloma collect in an hysterical style and produce malignant cells in bone marrow, in adults the bone marrow is mostly in the sternum and iliac bone, pockets are present in all bones, so myeloma- cytes can grow in every bone of body, even vertebrate and skull, ribs, except joints, tiny bones of feet hands and because of very little bone marrow[3]. Patients of multiple myeloma can develop recurring infections as the immunolglobulins must resist different microorganisms, the urinary tract, lung, bronchus and skin may be the first sign of the multiple myeloma[4]. Multiple myeloma forms about ten percent of blood tumors, it consists of pre-cancerous condition named gammopathy of monoclonal antibodies of uncertain importance, in about 3% in age 50 years, some have an intermediate level multiple myeloma that carries a transformation risk of 10% /yr. for five years later, and 1% /yr. for following ten yrs. (collective possibility of 75% at 15 yrs., the medium period at identification ranged (65-70)[5]. The multiple myeloma patients suffer from pain in bone, weakness, loss of appetite, frequent of infection and paresthesia with pneumonias and UTIs with *Streptococcus spp., Haemophilus, Escherichia coli* and other causative agents, also fever, hepatomegaly, splenomegaly, pleural and pulmonary involvement and renal insufficiency caused by cast nephropathy, hypercalcaemia, hyperuricemia and anaemia[6]. Anaemia in multiple myeloma patients, usually Normocytic Normochronic is shown in seventy –five percent of studied sample, rouleaux formation of erythrocytes also seen circulated plasma cells and leuco-erythroblastic image are rarely appeared, since antibodies titer elevation, erythrocyte

Table 1: Association of gender with multiple myeloma patients and control group.

	Gender		
Studied group	Male	Female	Total
Patients	25	22	47
Control	11	18	29
Total	36	40	100%

P value ≥ 0.05 Non significant

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Table 2: Association the types of immunoglobulins in multiple myeloma patients and control group.

	Igs types				
Studied groups	IgA	IgM	IgG	negative	Total
Patients	6(7.8%)	2(2.6%)	33(43.5%)	6(7.8%)	47(61.8%)
Control	0	0	0	29(38.1%)	29(38.2%)
Total	6(7.8%)	2(2.6%)	33(43.5%)	35(46.1%)	100%

P .value =0.001 HS

Table 3: Types of light chains in multiple myeloma patients and control group.

Studied groups	Kappa	Lambda	Negative	Total
Patients	22(28.9%)	20(26.3%)	5(6.6%)	47(61.8%)
Control	0%	0%	29(38.2%)	29(38.2%)
Total	28.9%	26.3%	44.8%	100%

P .value =0.001 HS

sedimentation rate is high[7]. Ordinary plasmocytes initiate one of five class of antibodies, whole antibodies is found in urine but in decreased concentrations, in numerous patients, management of construction and attach heavy and light chains in the abnormal plasma cells is missing, non –attached chains (light) invade the blood and are discharge quickly in urine[8]. This study was aimed to determine the type of antibody that are seen in sera protein electrophoresis, also level of protein in the sera of patients by electrophoresis (immunofixation technique).

MATERIALS AND METHODS

This study was conducted 47 patients (25 males & 22 females) suffering from multiple multiple myeloma from Medical city in Baghdad during the period (October 2017-February 2018), their ages ranged from 41-72 years, they were 27 males and 20 females. Besides 29 healthy humans as control group, their ages ranged; 39-70 years (11 males & 18 females).

Sampling

Fasting blood specimens were collected from each patient and control group, permitted to clot and sera were isolated then centrifuged. kept at (-20° C) until time testing.

Immunoglobulins (IgA, IgG & IgM) were measured in multiple myeloma and control group.

The free light chains (Kappa, Lambda) were also measured. Total protein, albumin, alpha -1, alpha -2, beta and gamma levels have been tested.

The immunofixation technique was used to detect and typing of by two steps:

First step includes deposit the antibodies present in urine otherwise sera a gel, followed by isolation the antibodies depending on differences of electrophoresis mobility by rendering them transfer according to the effectiveness of an electrical ground. When the immunoglobulins are isolated, movement depends on the weight and charging of antigenic particles.

Next step depends on using immunofixation method that needs electrophoretic force to move the proteins of the serum in duplicate, finally, particular antiimmunoglobulin anti-sera have used to deal each. duplicate. Anti-sera are not located in a canal like electrophoresis, other than, addition to each migration lane was individually.

Existence of antibodies (monoclonal type) caused in the manifestation of a thin band following stain reactive precipitate. Statistical analysis was performed to assess significant associations. P. values fewer than 0.05 be consider significant).

Table (1) shows distribution of multiple myeloma patients according to gender. It was found that no significant differences between male and female patients compared with healthy people.

Table (2) shows the types of antibodies, the positive titer of antibodies IgA 6 (7.8%), IgM 2(2.6%) and IgG 33(43.4%), while negative antibodies 6(7.8%), it is highly significant ($P < 0.001$), while all antibodies in control group are negative.

Table (3) showed in presence of Kappa and Lambda chains in multiple myeloma patients; 22(28.9%),20(26.3%) respectively while 5(6.6%) was negative, it is highly significant difference between patients and healthy control.

Table (4) shows the alpha-1 level in multiple myeloma patients 28(36.9%) normal,19(25%) abnormal, it is considerably different P $less\ than$ 0.001

Table (5) showed the level of alpha-2 in multiple myeloma patients: normal 33(43.4%), abnormal 14 (18.5%), it is very considerable difference.

Table (6) shows the level of beta – in the sera of multiple myeloma patients: normal 38(50%), abnormal 9(11.8%), notably variation $P < 0.05$ in comparison to healthy patients.

Table (7) shows the level of gamma in multiple myeloma patients, normal 10 (13.1%), abnormal 37(48.7%), it is highly significant difference ($P < 0.001$) comparing to healthy control.

Table (8) shows the level of albumin in sera of patients of multiple myeloma, normal 19(25%), abnormal 28 (31.8%), it is extremely important difference ($P < 0.001$) compared with control group.

Table (9) shows levels of total protein in sera of multiple myeloma patients normal 29(38.2%), abnormal 18 (23.6%), it is greatly important: $P < 0.001$ comparing to healthy group.

DISCUSSION

The immune mechanism of monoclonal gammopathy is

Table 4: Alpha-1 level in the sera of multiple myeloma patients and control group.

Alpha-1			
Studied groups	Normal	Abnormal	Total
Patients	28(36.9%)	19(25%)	47(61.9%)
Control	29(38.1%)	0 (0%)	29(38.1%)
Total	57(75%)	19(25%)	76(100%)

P. value =0.000 < 0.001 HS

Table 5: Level of alpha-2 in the sera of multiple myeloma patients and control group.

Alpha-2			
Studied groups	Normal	Abnormal	Total
Patients	33(43.4 %)	14(18.5%)	47(61.8%)
Control	29(38.2%)	0 (0%)	29(38.2%)
Total	62(81.6%)	14(18.5%)	76(100%)

P-- value = < 0.001 HS

Table 6: Level of beta- in the sera of multiple myeloma patients and control group.

Beta			
Studied groups	Normal	Abnormal	Total
Patients	38(50%)	9(11.8%)	47(61.8%)
Control	29(38.2%)	0 (0%)	29(38.2%)
Total	67(88.2%)	9(11.8%)	76(100%)

P. value =0.007 < 0.05 HS

Table 7: Level of gamma in the sera of multiple myeloma patients and control group.

Gamma			
Studied groups	Normal	Abnormal	Total
Patients	10(13.1%)	37(48.7%)	47(61.8%)
Control	29(38.2%)	0 (0%)	29(38.2%)
Total	39(51.3%)	37(48.7%)	76(100%)

P. value =0.000 < 0.001 HS

Table 8: Level of albumin in sera of multiple myeloma patients and control group.

Albumin			
Studied groups	Normal	Abnormal	Total
Patients	19(25%)	28(36.8%)	47(61.8%)
Control	29(38.2%)	0 (0%)	29(38.2%)
Total	48(63.2%)	28(36.8%)	76(100%)

P. value =0.000 < 0.001 HS

Table 9: Level of total protein in sera of multiple myeloma patients and control group.

Albumin			
Studied groups	Normal	Abnormal	Total
Patients	29(38.2%)	18(23.6%)	47(61.8%)
Control	29(38.2%)	0 (0%)	29(38.2%)
Total	58(76.4%)	18(23.6%)	76(100%)

P. value =0.000 < 0.001 HS

not well understood[9]. Monoclonal immunoglobulins type immunoglobulin M aggregate is detected in the wide last lamellae of myelin fibers and in myelin remains enclosed in macrophages and Schwann cells, the causes & explanations of monoclonal neuropathy such as: Heriditary, alcoholism, diabetic patients & treatment by drugs should first be considered and excluded, there was no specific test that can be done to distinguish between true causal association and an incidental one. Generally; young people, most than the connection is reasonable, since the occurrence of M protein in people less than 50 years of age[10].

Characterization of multiple myeloma be the malignancy of B-cells is demonstrated by the increase of plasma cells clonal population in bone marrow producing a monoclonal antibodies, stromal cells of bone marrow forming numerous pro- inflammatory factors that have an essential function in pathophysiology of myeloma syndrome[11].

Monoclonal proteins detection and diagnosis has developed in latest years, cellulose acetate was replaced with agarose for routine serum protein electrophoresis to find a high resolution and reproductivity[12].

The immune mechanism is consideration to be a direct effectiveness of - proteins M on the marginal nerve, resulting in a process of demyelinating, about twenty-five patients with Waldenstrom macroglobulinemia and neuropathy establish that all the cases where the immunoglobulin M shown activity towards myelin[13]. The immunoglobulin type M monoclonal gammopathy related tangential neuropathy presents as distal acquired demyelination, M-proteins symmetric neuropathy, it is considered a variant of chronic inflammatory demyelinating polyradiculoneuropathy[14]. There are differences in the clinical presentation of neuropathy associated IgM proteins compared with reported to be associated with IgG or IgA proteins[15].

Concentrations of monoclonal protein did not effectively associate with anion space, the space in IgG or IgA monoclonal gammopathies did not effect by the concomitant clonal free light chain concentration[16]. Heavy and light chains which independently recognize the different light chain types of each immunoglobulin class can produce original antibodies (IgG_k, IgG_T, IgA_k, IgA_T)[17]. These light chains allowed precise quantification of the involved antibody for affected isotype patients, also of the polyclonal and monoclonal antibodies of the some isotype; IgG_k/ IgG_T which evaluate heavy-light chains ratios[18].

The finding presented that light chains indicate using for verify and measure antibodies, premature decline, discover the immune reactivity and assist in credit of minimum remaining syndrome, this finding agreed Mills *et al*.,(2016) ;Milan *et al*.,(2017)[19,20] which relies upon immunoglobulin ratio for identifying and quantifying monoclonal components ,represent additional tool for diagnosis and monitoring of patients.

Increased level of total protein and and globulin in the sera of multiple myeloma patients are clues to diagnose of the disease, also showed hypoalbuminemia in the patients, those results agree with Karen *et al*.,(2011)[21]. The fractional excretion of both Kappa and Lambda free light chains was varied between different renal diseases such as diabetec nephropathy and non-diabetec nephropathy, this may relate to differences in proximal

tubules functions. The patients with non- diabetic glomerular disease comprise no elevated free light chains levels in urine, nevertheless demonstrate a considerable relation linking albumin/ creatinine ratio in urine plus free light chains which were negligible in others , that could reveal the restricted ability of re-absorption in tubules of core portions, that well-matched with earlier study to demonstrate that the proximal and distal canals re-absorption this protein preferred towards free light chains[22].

In this study describes monoclonal free light chains in sera of multiple myeloma patients, these data provide to assess the contribution systemic inflammation and renal injury in patients of multiple myeloma.

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