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Original Research Article

Prevalence of multiple myeloma and its complication in a tertiary medical college at Calicut district, India

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ABSTRACT

Background: Multiple myeloma is a blood cancer that develops in the bone marrow, which is soft, spongy tissue found in the center of many bones where blood cells are produced. In myeloma, plasma cells, which are normal antibody-producing cells, transform into cancerous myeloma cells. The objectives of this study was the prevalence and complications of multiple myeloma.
Methods: A cross sectional study was conducted in a tertiary hospital at Calicut. Semi structured questionnaire was used to study the prevalence and associated complications of multiple myeloma. History taking, physical examinations and investigations like hemoglobin estimation, peripheral smear, electrophoresis, renal function test, calcium estimation, X-ray of thoracic, lumbar spine, humerus, hip region was done. There was also an attempt to find co-morbidities hypertension, diabetes mellitus and neurological abnormalities. The variables was entered into excel and data were expressed in tables.
Results: The prevalence of multiple myeloma in Calicut was found to be 77.90% of the bone marrow results were consistent with multiple myeloma. Urine Bence jone protein was positive for 22.9% of cases. Electrophoresis was done and M Band was seen positive for 78.6%. Serum blood urea value was more for 25.7% patients and 22.95% had elevated serum creatinine value. Spine compression was found among 41.4% and osteoporosis was seen in 21.4% patients. Hypertension was seen among 90% cases and Diabetes Mellitus in 4.7% of males.10 % of the patient has valvular heart disease.
Conclusion: The study was able to find out the prevalence and project complications of multiple myeloma at Calicut. As there are cases in the district, present medicos who are the future doctors should be trained appropriately to diagnose and treat the disease.

Keywords: Complications, Diabetes, Hypertension, Multiple myeloma, Osteoporosis, Prevalence, Spine compression

INTRODUCTION

Multiple myeloma is the malignant proliferation of plasma cells which involves more than 10% of the bone marrow. It is characterized by anemia, monoclonal protein in the serum or urine or both, abnormal bone radiographs and bone pain. Global prevalence of the disease is 2, 10,697 or 4.3/1, 00,000 population and India is 11,602 or 1.4/1, 00,000 population. The worldwide mortality rate due to Multiple myeloma is 72,453 which accounts for 1% of all cancer related deaths and India it accounts for about 5,900 deaths every year.[1,2]

Professor Otto Kahler described a case in the year 1889, involving a 46-year-old physician with multiple myeloma and described the disease in a major way. He explained about the skeletal pain, albuminuria, pallor, anemia, a precipitable urinary protein, and the findings on necroscopy and linked these findings as part of a clinical syndrome, which bears his name Kahler disease.

The site of production of the Bence Jones protein was postulated as bone marrow by Weber in the year 1898. Wright emphasized that multiple myeloma arose specifically from plasma cells of the marrow in 1933. In 1917 and 1921, respectively, Bence Jones proteins in the bloodstream was recognized by Jacobson and Walters and concluded that the Bence Jones protein was probably derived from blood proteins through the action of the abnormal cells in the bone marrow.[2]

There are multisystem involved as complication of the disease. In 1928, Geschickter and Copeland documented a higher incidence in men than women and an overall survival of about 2 years. They emphasized involvement by the tumor of the skeletal trunk, pathologic fractures of the ribs, Bence Jones proteinuria in 65% of cases, backache with early paraplegia, anemia in 77% of cases, and chronic renal disease.[3] The bone complications associated with multiple myeloma include bone pain, pathologic fractures, hypercalcemia of malignancy and cord compressions. The principal pathophysiology of bone disease in multiple myeloma is a shift in the balance of bone remodeling toward bone resorption. [4]

Complications such as renal failure, infections, anemia, lytic bone lesions and amyloidosis lead to morbidity as well as mortality.[5] Shortages of red blood cells, white blood cells, and blood platelets are common in multiple myeloma and can lead to anemia, leucopenia, and thrombocytopenia. High levels of calcium in the blood (hypercalcemia) can cause extreme thirst, leading to drinking a lot, increased urination, dehydration, kidney problems and even kidney failure. Also, it can cause constipation, abdominal pain, loss of appetite, weakness, feeling drowsy, and confusion. If the level of calcium gets high enough, you can even slip into coma. If myeloma weakens the bones in the spine, they can collapse and press on spinal nerves and can head to spinal cord compression and cause sudden severe back pain, numbness, muscle weakness in the legs.

The abnormal proteins produced by myeloma cells are toxic to nerves which can lead to weakness and numbness and present as “pins and needles” sensation which is called peripheral neuropathy. In few cases, large amounts of myeloma protein can cause the blood to “thicken.” (Hyper viscosity). It can slow blood flow to the brain and cause confusion, dizziness. Weakness on one side of the body and slurred speech can occur. Myeloma protein can damage the kidneys, which may be seen on a blood test or a urine test. As the kidneys start to fail, they lose the ability to get rid of excess salt, fluid, and body waste products. This can lead to symptoms such as weakness, shortness of breath, itching, leg swelling.[6]

Complications such as renal failure, infections, anemia, lytic bone lesions and amyloidosis lead to morbidity as well as mortality.[7] Patients with amyloidosis also mimic myeloma with renal problems and nerve damage. The heart may enlarge and become weaker, that fluid builds up in the lungs, making them feel short of breath, which can lead to congestive heart failure. Fluid may build up in the legs and feet, forming edema.

The patient may feel the liver enlarged and below the right ribs which can get large and can press the stomach, making the patient feels full after eating only a small amount of food. When amyloid builds up in the tongue it can get larger and can have problems in swallowing and breathing difficulty (sleep apnea). Changes in the color or texture of skin can occur, easy bruising, and bleeding into the skin around the eye’s raccoon eyes is also possible.[6]

In this part of country, there are limited data available on the prevalence and complications of Multiple Myeloma at Southern Kerala. So, this study would help to quantify the data in this regard.

METHODS

The study was conducted at a tertiary center, Government Medical College, Calicut. The research team consisted of Principle investigator, two Assistant Researchers, Pathologist, technicians of X-ray, laboratory. The patient who came to the Outpatient Department of General Medicine, Department of Calicut Medical who fitted to the criteria of diagnosis were designated as cases of Multiple Myeloma. The sampling method used was convenient sampling.

The researcher conducted the study with semi structured questionnaire and recorded Clinical History, General and Clinical Examination along with Investigations like blood examinations, X Ray-Chest, Humerus, femur. Urine Bence jones proteins, immune electrophoresis of urine or blood for type of protein, skeletal survey for characteristic punched out lesion, bone marrow examination for increased plasma cells with morphological abnormalities, electrophoresis for demonstration of paraprotein were also done .The diagnosis of Multiple myeloma was based on major and minor criteria.[8] The variables was entered into excel and frequency and percentage were depicted using tables. Written consent has been taken from individual patients to conduct the study.

The study was a cross sectional study and the duration of study was one year. The objective of study was to assess the prevalence of Multiple Myeloma and delineate the various modes of presentations and complications of the disease.

RESULTS

The prevalence of Multiple Myeloma in Calicut was found to be 77. Out of 77 patients, bone marrow results were consistent with Multiple myeloma for 63 patients (90%) and there was not much difference on the basis of gender. Renal biopsy was positive for 3.7% of females of the study sample. Plasma Cytoma biopsy was positive for males 16.3% and 7.4% females. Urine Bence jone protein was positive for 22.9 % of cases. Electrophoresis was done and M Band was seen positive for 78.6%. 25.7% of patients had serum blood urea value more than 45 and 22.95% had serum creatinine value more than 1.2. Albumin globulin reversal value was seen higher in 80% of cases.

Table 1: Showing results of various investigations of patients with Multiple Myeloma.

Bone Marrow	Male		Female		Total	
	Number	%	Number	%	Number	%
Consistent with myeloma	39	90.7	24	88.9	63	90
Normal	5	11.6	2	7.4	7	10
Renal Bx	0	0	1	3.7	1	1.4
Plasma Cytoma Bx +ve	7	16.3	2	7.4	9	12.9
Urine Albumin +ve	9	20.9	5	18.5	14	20
Urine BJP +ve	8	18.6	8	29.6	16	22.9
M Band +ve	36	83.7	19	70.4	55	78.6
Blood Urea- <40	31	72.1	22	81.5	53	75.7
>40	12	27.9	6	22.2	18	25.7
Serum Uric Aid						
Normal	43	100	24	89	67	96
Decreased	0	0	3	11	3	4.3
Serum Creatinine						
<1.2	35	81.4	21	77.8	56	80
>1.2	10	23.3	6	22.2	16	22.9
Normal Serum Creatinine, Increased Blood Urea	2	4.7	1	3.7	3	4.3
Albumin Globulin Reversal	37	86	19	70.4	56	80
Hypergammaglobulinemia	41	95.3	19	70.4	60	85.7
Hypergammaglobulinemia without AG Reversal	4	9.3	0	0	4	5.7

Table 2: Showing frequency and percentage of fractures of patients with Multiple Myeloma.

Fractures	Male		Female		Total	
	Number	%	Number	%	Number	%
Spine compression	20	46.5	9	33.3	29	41.4
Trochantric	0	0	23	11.1	3	4.3
Humerus	2	4.7	0	0	0	2.9
T+H	0	0	1	3.7	1	1.4
Pelvis	1	2.3	0	0	1	1.4
Osteoporosis	7	10	8	29.6	15	21.4
Osteosclerosis	0	0	1	3.7	1	1.4

Spine Compression was seen among 41.4% of the subjects. Trochentric fractures were only present in females 11.1%. Only 2 males had humerus fracture and only one female had both Trochentric and humerus fractures. Osteoporosis was seen in 21.4% and only one female had osteosclerosis. Hypertension was seen among 90% of the patients and there was not much difference between gender whereas Diabetes Mellitus was only seen in 4.7% of males among the patients. 10% of the patient has valvular heart disease and only one female patient has Ischemic heart disease.

Splenomegaly was seen in 16.3% of males and 7.4% of female patients. 8.6% 0f patients had paraparesis and only 4.7% males suffered from paraplegia. 2.3% males has quadriplegia and 3.7% females has diplopia.

Table 3: Depicting frequency and percentage of other findings of patients with Multiple Myeloma.

Other Findings	Male		Female		Total	
	Number	%	Number	%	Number	%
Hypertension	39	90.7	24	88.9	63	90
Valvular Heart Disease	5	11.6	2	7.4	7	10
Ischemic Heart Disease	0	0	1	3.7	1	1.4
Splenomegaly	7	16.3	2	7.4	9	12.9
Hepatomegaly	9	20.9	5	18.5	14	20
COPD	8	18.6	8	29.6	16	22.9
Diabetes Mellitus	2	4.7	0	0	2	2.9
Paraparesis	4	9.3	2	7.4	6	8.6
Paraplegia	2	4.7	0	0	2	2.9
Quadriplegia	1	2.3	0	0	1	1.4
Diplopia	0	0	1	3.7	1	1.4

DISCUSSION

Multiple myeloma forms with a multistep process with help of exogenous stimuli which induce cytogenetic changes in the B-cell lineage at the lymph node. The multiple myeloma cells establish itself in the bone marrow, adhering to stromal cells where it inhibits osteoblastic activity and osteocalcin production. The multiple myeloma cell-stromal cell interaction stimulates production of interleukin-6 (IL-6) and several other osteoclast-activating factors. Increased osteoclastic activity combines with inhibited osteoblastic activity to produce the skeletal complications of multiple myeloma, including osteoporosis, painful lytic lesions and hypercalcemia of malignancy.[4]

A study done by Fousad et al, on Multiple Myeloma patients found that (18.8%)had hypercalcemia, (21.9%) had elevated serum creatinine levels, low serum albumin 20 (62.5%), Urine Bence-Jones proteinuria 3 (9.4%), Serum protein electrophoresis showing M band 30 (94%).[6,7,9] Another study conducted by Kaur et al, found that bony pain was the most common presenting complaint followed by anemia, raised serum creatinine levels, high serum lactate dehydrogenase and C-reactive protein levels. Plasmablastic morphology was seen in 60% patients with diffuse marrow involvement being the most common pattern.[10]

Prakash J et al, found that Multiple myeloma contributes to 1.93% of total ARF cases (26/1342) over a period of thirteen years. The clinical manifestations of patients were anemia (100%), Bence Jones proteinuria (80%), "M" peak in serum electrophoresis (69%), lytic bone lesions (62%), "M" peak in urine electrophoresis (54%), body pain (58%), plasma cells more than 20% in bone marrow aspirate (38%). Oliguric ARF was seen in 73% patients. The precipitating factors of ARF identified were hypercalcemia (31%), infection (23%), volume depletion (19%) and NSAIDs in (15%).[11]

In this study, 84.3% of patients were anemic. Urine Bence jone protein was positive for 22.9% of cases. Electrophoresis was done and M Band was seen positive for 78.6 %.

In a study conducted by Kaur et al, Ninety-eight percent of patients have an M-protein in the serum or urine at the time of diagnosis. Skeletal X Rays were abnormal in nearly 80% and Renal insufficiency (creatinine >or=2 mg/dL) is present in one-fourth. In the present study 25.7% of patients had Serum Blood urea value more than 45 and 22.95% had Serum Creatinine value more than 1.2.Albumin globulin reversal value was seen higher in 80% of cases.[10]

Diwan et al, found that among skeletal involvement, 19 patients (85%) had osteolytic lesions, 8 patients (40%) had generalized osteoporosis, 7 patients (35%) had pathological fractures. Spine and skull were the common sites of involvement 60% and 55% respectively. One patient did not have skeletal involvement. Bone marrow examination revealed the presence of more than 50% plasma cells in 9 cases (45%), 7 patients (35%) had 10-30% plasma cells 4 patients (20%) had plasma cells in the range of 30-50%. In this study, it was found Spine Compression was seen among 41.4 % of the subjects. Trochentric fractures were only present in females 11.1%. Only 2 males had humerus fracture and only one female had both Trochentric and humerus fractures. Osteoporosis was seen in 21.4% and only one female had osteosclerosis.[12]

Physical examination is most helpful for identifying signs other than symptoms to be directed towards diagnosis. Most patients with multiple myeloma have normal physical examination findings on presentation. Laboratory evaluation in a patient with suspected multiple myeloma has the highest diagnostic yield. Prognosis has been based on staging, which combines clinical factors, including the amount of M-protein,

serum hemoglobin level, serum calcium level, number of lytic bone lesions on a skeletal radiographic survey and renal function.[13] The most significant factors are the level of b2-microglobulin, a light chain protein that is elevated in lymphoproliferative diseases,[14] and serum albumin level. Another important prognostic factor is C reactive protein, a surrogate marker of IL-6, an osteoclast-activating factor.[15]

CONCLUSION

The findings had helped to quantify the prevalence of Multiple myeloma, i.e. 77. The study had showered light to various complication as part of the disease. They are anemia, elevated urea, creatine level, spine compression, fracture trochanter, fracture humerus, fracture pelvis, osteoporosis, osteosclerosis. Medical students should be trained to treat multiple myeloma with competence.

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