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RENAL MANIFESTATIONS IN HEMATOLOGICAL MALIGNANCIES: A PROSPECTIVE STUDY

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ABSTRACT

Background: The renal complications of cancer have become one of the important determinants of prognosis in patients with malignancies and combined efforts of the Hemato-Oncologist and the Nephrologist are required for care of these patients in view of the wide spectrum of syndromes that may occur. These renal complications of hematological malignancies are often preventable or reversible with prompt diagnosis and treatment.

Aims: To study the renal manifestations in haematological malignancies.

Material and Methods: The study entitled "Renal manifestations in hematological malignancies" was carried out in 60 patients with established diagnosis of a hematological malignancy admitted in different departments in Government Medical College, Jammu and associated Hospitals. This prospective study was conducted over a period of one year from 1st November 2008 to 31st October 2009. After confirmation of diagnosis all hematological malignancy patients were evaluated for clinical, biochemical, urinary, ultrasonographic and/or computed tomographic evidence of renal involvement, supported by histopathological confirmation (wherever feasible and indicated).This assessment was done at the time of admission, before institution of specific treatment protocol for each patient, in the study group.

Observations: To summarize the important observations in the study, we found that significant renal enlargement of 1-4cms was observed in 19 cases and majority of these had bilateral enlargement. Commonest metabolic abnormality was hypokalemia (12 cases) followed by hypophoshatemia observed in 11 patients, 9 patients had hyperuricemia, 8 hypercalcemia and 8 patients had hypocalcemia The other metabolic abnormalities observed in the patients of hematological malignancies included hyponatremia in 7, hyperkalemia in 7, hypouricemia in 4 and hyperphoshatemia in 1 patient.

Conclusion: Renal involvement by tumor, although rare can sometimes be the sole manifestation of a hematological malignancy before it is detectable by routine methods. It can present as renal enlargement, obstructive uropathy, glomernlonephritis, tubular abnormalities or as paraneoplastic syndromes, so by keeping knowledge of these possibilities these tumor related catastrophes can be prevented from occurring or halted before these can endanger the life.

Key Words: Hypokalemia, Nephromegaly, Paraneoplastic, Hperphosphatemia, Glomernlonephritis, Hematological

INTRODUCTION

The renal complications of cancer have become one of the important determinants of prognosis in patients with malignancies and combined efforts of the Hemato-Oncologist and the Nephrologist are required for care of these patients in view of the wide spectrum of syndromes that may occur. The spectrum of diseases in hematological malignancies can be in various forms namely, acute renal failure (pre-renal, renal, post-renal), chronic renal failure, glomerulopathies, tubulointerstitial diseases, treatment related nephropathies, fluid and electrolyte abnormalities and acid-base disturbances which can be tumor related or treatment related. These renal complications of hematological malignancies are often preventable or reversible with prompt diagnosis and treatment (1).

The renal complications of malignancies in addition to paraneoplastic glomerulopathy can occur either due to: a) mechanical (direct) effect of tumor in the form of

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infiltration of renal parenchyma, obstructive uropathy, compression of renal vessels, b) metabolic (indirect) effects in the form of nephrocalcinosis, myeloma cast nephropathy, electrolyte disturbances, disseminated intravascular coagulation and thrombotic microangiopathy or c) treatment induced effects in the form of tumor lysis syndrome, lithiasis and uric acid nephropathy, radiation nephropathy, drug induced tubulointerstitial disease and thrombotic microangiopathy and mesangiolysis(2).

The association of nephrotic syndrome and cancer is most striking in the patients with hematological neoplasias particularly in mixed cellularity type of hodgkins disease (3). Proteinuria tend to reappear with relapse of lymphoma, supporting the statement that nephrotic syndrome is a consequence of malignant disease and not a coincidence (4). Renal failure is the second most common cause of death in cases of multiple myeloma. Renal failure in multiple myeloma can be related to abnormal paraproteins, hypercalcemia, hyperuricemia, dehydration, the use of intravenous contrast agent, nephrotoxic drugs and many other factors(5).

Considering the above facts, we conducted a prospective study to know the pattern of renal manifestations in patients with hematological malignancies like lymphomas, leukemias and multiple myeloma who were admitted in Government Medical College, Jammu and associated Hospitals.

AIMS AND OBJECTIVES

To study the renal manifestations in hematological malignancies

MATERIAL AND METHODS

The study entitled "Renal manifestations in haematological malignancies" was carried out in 60 patients with established diagnosis of a haematological malignancy admitted in different departments in Government Medical College, Jammu and associated Hospitals. This prospective study was conducted over a period of one year from 1st November 2008 to 31st October 2009. All the eligible patients were explained the purpose of study and were invited for participation. All leukemic patients were characterized as per FAB classification whereas lymphoma patients were subdivided on histological basis (working formulation).

After confirmation of diagnosis all haematological malignancy patients were evaluated for clinical, biochemical, urinary, ultrasonographic and/or computed tomographic evidence of renal involvement, supported by histopathological confirmation (wherever feasible and indicated.) This assessment was done at the time of admission, before institution of specific treatment protocol for each patient, in the study group.

Definitions:

Leucocyturia, was defined if urine contained more than 3 leucocytes per high power field.

Hematuria, was defined when urine contained more than 3 erythrocytes per high power field.

Poteinuria, was taken when 24 hour urinary protein concentration was more than 150 mg/dl.

Urinary sodium was taken as low (hyponatremia) and high (hypernatremia) when the values were below 20 mmol/l and above 110 mmol/l respectively.

Urinary potassium was taken as low (Hypokalemia) and high (Hyperkalemia) when the values were below 12mmol/l and above 75mmol/l respectively .

Urinary creatinine below 30mg/dl and above 125mg/dl was taken as low and high respectively.

Urinary calcium was taken as low (Hypocalcemia) and high (Hypercalcemia) when the values were below 42mg/dl and above 353mg/dl respectively.

Urinary phosphorus values below (Hypophosphatemia) 20mg/dl and above (Hyperphosphatemia) 60mg/dl were taken as low and high respectively.

Similarly urinary uric acid values below 7.5mg/dl and above 49.5mg/dl were taken as low and high respectively.

Clinical evaluation

The study subjects were assessed for renal involvement by examining for pedal edema, facial puffiness , hypertension, renal enlargement / renal mass and renal angle tenderness.

Biochemical evaluation: All patients in this study had undergone urea and creatinine estimation before treatment protocol was started. The estimations were done by using Diacetyl monoxime (DAM) method and alkaline picrate method respectively. Besides, all the patients were evaluated for hypo- and hyperkalemia, hypo-and hyperphosphatemia, hypo-and hypercalcemia, hypo-and hypernatremia and for hypo- and hyperuricemia. Serum electrolytes and other biochemical parameters, needed in the study, were estimated by Dade's Behring Dimension AR automated analyzer. Arterial blood gas analysis was done by using AVL blood gas analyzer.

Urinary parameters: The patients in this study had undergone the analysis for the following urinary parameters:

1. Complete Urinalysis for Gross and microscopic examination, Urinary sugar by Benedict's qualitative glucose test, Urinary proteins by heat and acetic acid test/ sulphosalicylic acid test.
2. 24 hour urinary protein estimation was done by using Esbach's quantitative method. On the basis of proteinuria, patients were divided into two groups:-
   Group-a):- patients with non-nephrotic poteinuria with urinary proteins less than 50mg/kg body weight/day
   Group-B):- Patients with nephrotic proteinuria with urinary proteins more than 50mg/kg body weight/day.
3. Bence Jones protein detection was done by heat and sulphosalicylic acid.
4. Urinary sodium, potassium, calcium, phosphorus, uric acid and creatinine estimation was done by using Dade's Behring Dimension AR automated analyzer.

In hyponatremic patients the fractional excretion of sodium ($FENa^+$) was calculated from the equation:

$$FENa^+ (\%) = \frac{(\text{urine } Na^+ \text{ X Serum creatinine})}{\text{Serum } Na^+ \text{ X Urinary creatinine}} \times 100$$

A fractional excretion of less than 0.1% was considered as indicative of hypovolemia (Rose BD, 1994). In hypokalemia patients the fractional excretion of potassium (FEK^+) was calculated from the equation:

$$FEK^+ (\%) = \frac{(\text{Urine } K^+ \text{X serum Creatinine})}{\text{Serum } K^+ \text{ X urine creatinine}} \times 100$$

A fractional excretion of more than 6.4% was considered as inappropriate Kaliuresis in hypokalemic patients(6) .Similarly the fractional excretion of phosphorus ($FEPo_4^{3-}$) in patients with hypophophatemia was calculated from the equation:

$$FEPo_4^{3-} (\%) = \frac{(\text{Urinary } Po_4^{3-} \text{ X serum Creatinine})}{\text{Serum } Po_4^{3-} \text{ X urine creatinine}}$$

A fractional excretion of more than 20% was considered as inappropriate (7).

Urinary uric acid to creatinine ratio of more than 1 in a patient of renal failure, suggested a hyperuricemic renal failure (8).

All the investigations were done in the Nephrology, Biochemistry and Hemotology laboratories of Government Medical College, Hospital Jammu.

Ultrasonography (USG): All patients in the study underwent USG examination, before and after specific treatment, by an experienced sonologist who was unaware of the study, in order to determine the kidney size (normal 9-12cm X 3-5cm X 2-3cm) and extent of renal, para-renal and peri-renal involvement by the disease process. Renal enlargement in these patients was taken as per reference values given by Emamian SA et al in 1993 (9). Ultrasonography was done by using grey scale real-time ultrasound scanner. For adults transducer with a frequency of 3.5 MHZ and for children 5-7 MHZ transducer was used.

Computed tomography:

Though highly sensitive than USG, in defining the renal lesions, size, extension and retroperitoneal involvement in hematological malignancies, was done only in few cases with suspicion or evidence of renal involvement.

Kidney biopsy:

Percutaneous kidney biopsy was done in patients with kidney involvement where consant for such procedure was given by the patients and / or their attendants. Indication was non-nephrotic range proteinuria, nephrotic syndrome, unexplained renal failure and renal enlargement.

Ethical committee clearance:

We undertook study after due clearance from the hospital ethical committee which composed of senior faculty members of the government medical college jammu. Regarding funding for the study, nothing was charged from the subjects as it was conducted in government hospital were all investigations charges were taken care of by the hospital. Only some medications were purchased by the patients in study which they had to buy otherwise also for their management and not related to nature of study itself.

Observations:

Renal manifestations in hematological malignancies in 60 consanted patients were studied for a period of 1 year from Ist. November 2008 to 31st October 2009. There were 42 males and 18 females in the study population. The age of subjects ranged from 3 to 75 years (mean 43.12 years). All of these patients were admitted in Government Medical College, Jammu and associated Hospitals, in different departments. Of these 60 patients 14 had lymphoma, 36 leukemia and 10 had multiple myeloma Fig.1. In the lymphoma group 5 had Hodgkins disease and 9 had non-Hodgkin's lymphoma, including 1 primary bone lymphoma. Out of 36 leukemic patients, 15 had acute myelocytic leukemia, 11 acute lymphoblastic leukemia, 8 chronic myelocytic leukemia and 2 had chronic lymphocytic leukemia Table 1.

Our observations were diverse as the renal complications in hematological malignancies were concerned depending upon the type of hematological malignancy (Table 2). With respect to hodgkins lymphoma out of 5 patients, 1 patient had clinical evidence of anasarca and his urinalysis revealed nephrotic proteinuria, dysmorphic red blood cells and red cell casts. Renal histopathology of this patient was related to minimal change disease. One

of the 5 patients had acute renal failure who on ultrasonography revealed bilateral renal enlargement with irregular contours but no evidence of dilated collecting system or retroperitoneal lymphadenopathy. Out of 9 patients of NHL, two patients had non-nephrotic proteinuria and 2 others had azotemia. Ultrasonography carried out in all these patients revealed bilateral nephromegaly in 2 patients and 1 more had unilateral enlargement of the kidney with a difference of more than 2 cms between the two sides. Renal size decreased significantly after appropriate treatment of the underlying disease and varied from 2 to 3.5 cms. Two Patients presented with oliguric renal failure and both of these patients revealed significant nephromegaly on ultrasound without any evidence of hydronephrosis.

In case of multiple myeloma, out of 10 patients in the study, 1 patient had generalized edema, 3 others had evidence of pedal edema and peri- orbital puffiness. 1 patient had nephrotic proteinuria and 2 others had trace proteinuria. In addition urinalysis revealed leucocyturia in 3, hematuria in 2 and casts in 2 patients. Bence Jones proteinuria was demonstrated in 4 Patients. Ultrasonography revealed nephromegaly in one patient which did not regress significantly after treatment and 1 more had bilateral renal calculi without any hydronephrosis. Three of these patients had renal failure at presentation and 1 more developed it after chemotherapy. In one patient of renal failure there was frequent history of analgesic intake (NSAID-induced) and no other evident cause for renal failure. Three patients had significant hypercalcemia, with normal serum phosphorus. Other metabolic abnormalities found in this group were hyperkalemia in 2 patients with renal failure, hypophosphatemia in one and hyponatremia in one patient. Arterial blood gas analysis revealed metabolic acidosis in 3 patients of acute renal failure.

In the CML group (8 patients) nephromegaly was found in 2 patients which reversed with treatment but renal biopsy couldn't be done in these patients because of bleeding manifestations and severe nature of illness. Non-nephrotic proteinuria with pedal edema was present in one of these patients who was in blast crisis phase. Urinalysis, in addition to proteinuria, in this patient revealed hematuria and granular casts. Arterial blood gas analysis of this patient revealed respiratory alkalosis. Among two patients of chronic lymphocytic leukemia in the study one patient had nephromegaly with no features of obstructive uropathy. This patient also had hyperuricemia and his urinalysis revealed sterile leucocyturia and microscopic hematuria.

In case of AML (15 patients) , we observed proteinuria in 6 patients, leucocyturia in 2, hematuria in 3, granuler casts in 3, Red blood cell casts in 1, and hyaline casts in 1 patient. One of the 15 patients had oliguria and 1 more had polyuria. Nephromegaly was observed in 4 patients which regressed in 3 patients after treatment by about 1.5- 2.5 cm. 2 patients had azotemia . Hypokalemia was the most frequent abnormality observed in 5 of 15 acute myeloid leukemic patients. Majority (4 of 6) of these hypokalemic patients were in AML-M4 subgroup. All these hypokalemic patients had fractional excretion of potassium more than 6.4%, suggestive of renal potassium wasting. Hypophosphatemia was observed in 4 patients and 3 of these had significant phosphaturia with fractional excretion of phosphorus more than 20 % while as one of these patients had phosphate excretion below normal range. Two patients had hyponatremia and one of these patients had fractional excretion of sodium (FENa) more than 3%, suggesting inappropriate natriuresis while as the other had FENa <1. The other metabolic abnormalities were hypocalcaemia in 3 patients, hyperuricemia in 1, hypouricemia in 2, hyperkalemia in 1, and hypercalcemia in 1 patients who also had increased urinary calcium and decreased phosphorous excretion. Two of 15 patients also had kaliuresis without hypokalemia. Arterial blood gas analysis revealed metabolic alkalosis in 3 patients, all of which had hypokalemia and one of these had hypercalcemia in addition. Metabolic acidosis was observed in one azotemic patients while as 2 patients had mixed acid-base disturbance.

In case of ALL patients urinalysis revealed urinary casts in 3 (granular in 2 and RBC Casts in 1 patient), hematuria in 2, leucocyturia in 1, and significant proteinuria in 2 patients. Seven out of 11 patients revealed nephromegaly on ultrasonography which regressed in 6 of these patients after chemotherapy. Hypokalemia was observed in 4 of 11 patients and 3 of these patients had renal potassium loss (Fractional excretion of potassium >6.4%). One of the 11 patients had kaliuresis but had no hypokalemia.

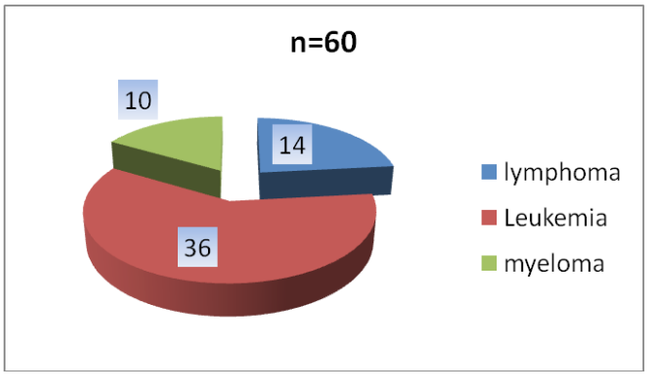

Figure 1: Major types of hematological malignancies.

Table 1: pattern of hematological malignancies in study group (n = 60)

Malignancy	N=60	%age
Lymphoma	14	23.33
HodgKin's Lymphoma (HL)	5	35.71
Non Hodgkin's lymphoma (NHL)	9	64.29
Leukemias	36	60
Acute myeloblastic leukemia (AML)	15	41.67
Acut lymphoblastic leukemia (ALL)	11	30.56
Chronic myeloid leukemia (CML)	8	22.22
Chronic lymphoblastic leukemia (CLL)	2	5.55
Multiple Myeloma	10	16.67

To summarise the important observations in the study, we found that significant renal enlargement of 1-4cms was observed in 19 cases and majority of these had bilateral enlargement. Nephromegaly was commonly observed in acute lymphoblastic leukemia group.Proteinuria was present in 18 cases and 2 of these had full blown nephrotic syndrome. Renal histopathology of 1 patient was suggestive of minimal change glomerulonephritis while as the other 1 had indirect evidence of amylodotic kidney. In rest of the 16 cases proteinuria was in non-nephrotic range.

Commonest metabolic abnormality was hypokalemia (12 cases) followed by hypophoshatemia observed in 11 patients, 9 patients had hyperuricemia, 8 hypercalcemia and 8 patients had hypocalcemia.

The other metabolic abnormalities observed in the patients of haematological malignancies included hyponatremia in 7, hyperkalemia in 7, hypouricemia in 4 and hyperphoshatemia in 1 patient.

Azotemia was observed in 10 patients and majority (4) of these patients were in myeloma group .

A total of 20 patients in this study had acid-base disturbance on arterial–blood gas analysis. The major acid–base disturbance observed was metabolic alkalosis, commonly observed in acute leukemia group..

In addition to proteinuria urinalysis of these malignancy patients revealed, urinary casts in 15, hematuria in 13 and leucocyturia in 12. These urinary abnormalities observed were most commonly in acute myeloid leukemia group. Three patients had tumor lysis syndrome in the study one of which was treatment related. All these renal complications of malignancies whether tumor or treatment related require care by a multidisciplinary team

DISCUSSION

The renal complications of malignancy have become one of the important determinants of prognosis. Hence early

Table 2: Renal and metabolic abnormalities in various type of neoplasias

PARAMETERS	LYMPHOMA (n=14)	LEUKEMIA (n=36)	MULTIPLE MYELOMA (n=10)	TOTAL
Renal enlargement	4 (28.57%)	14(38.89%)	1 (10%)	19(31.67%)
Proteinuria	3 (21.42%)	10(27.77%)	5 (50%)	18 (30%)
Hypophosphatemia	2 (14.29%)	8 (22.22%)	1 (10%)	11(18.33%)
Hypocalcemia	2 (14.29%)	6 (16.66%)	-	8 (13.33%)
Hypokalemia	1 (7.14%)	11(30.55%)	-	12 (20%)
Hyponatremia	2 (14.29%)	4 (11.11%)	1 (10%)	7 (11.67%)
Hyperphosphatemia	-	-	1 (10%)	1 (1.67%)
Azotemia	3 (21.4%)	3 (8.33%)	4 (40%)	10(16.67%)
Hyperkalemia	2 (14.29%)	2 (5.55%)	3 (30%)	7 (11.67%)
Hypercalcemia	2 (14.29%)	3 (8.33%)	3 (30%)	8 (13.33%)
Acidosis	1 (7.14%)	2 (5.55%)	3 (30%)	6 (10%)
Alkalosis	2 (14.29%)	6 (16.66%)	1 (10%)	9 (15%)
Mixed	1 (7.14%)	3 (8.33%)	1 (10%)	5 (8.33%)
Hypouricemia	1 (7.14%)	3 (8.33%)	-	4 (6.67%)
Peruricemia	3 (21.4%)	5 (13.89%)	1 (10%)	9 (15%)

diagnosis and effective management of these complications is necessary to improve survival and prognosis in these patients. In order to know the pattern of renal complications in hematological malignancies in our part of the world we conducted a study in different departments of GMC jammu. Out of total 60 patients included in the study, 19 (31.67%) patients showed enlarged kidneys on ultrasonography. None of these patients showed evidence of hydronephrosis. The renal enlargement was bilateral in majority of these patients (78.95%).The renal size regressed in the patients by 1 to 3.5 cms after appropriate treatment and this initial increase followed by decrease in size was related to renal infiltration of the kidneys by hematological neoplasias. Present study closely correlates with other reported series like Xiao JC (1997) and Martinez-Meldonado M (1966) (10) and (11), who reported renal infiltration in 34% and 42.3% cases respectively.

Out of 36 patients with various leukemias in the study, 14 (38.89%) showed nephromegaly due to leukemic infiltration. Our study closely correlates with the study of Khanna UB et al, 1985 (12) who reported renal infiltration in 42.85% of leukemia cases. Autopsy data by Norris HJ et al (1961) and Shapiro JH et al (1962) (13) and (14) observed renal invasion in 47-61% and upto 60% cases respectively. Diffuse parenchymal infiltration is most frequent pattern of invasion in acute leukemias but can be seen in non-Hodgkin's lymphoma also.

The association of nephrotic syndrome and cancer is most striking in patients with hematological neoplasias. Though it may occur in various hematological neoplasias but nephrotic syndrome is most common in Hodgkin's disease especially in mixed cellularity type (15).

In a study by Eagen JW and Lewis EJ in 1977 (16) about 45% of cases of nephrotic syndrome occur concurrently with Hodgkin's disease, 10% precede the lymphoma and in 40-50% nephrotic syndrome is manifested after the tumor is diagnosed. However, in the present study only 1 out of 5 cases of Hodgkin's lymphoma had nephrotic syndrome and renal biopsy was suggestive of minimal change glomerulonephritis. This case of nephrotic syndrome was diagnosed concurrently with the diagnosis of Hodgkin's disease, although it might have preceded the lymphoma but history favoured concurrent occurrence. The disappearance of nephrotic proteinuria after chemotherapy most probably favours the paraneoplastic nature of nephrotic syndrome and not a coincidental phenomenon.

Khanna UB et al in 1985 (17) reported that all of their patients with renal involvement had Bence Jones proteinuria. In our study, Bence-Jones proteinuria was present in 4 (40%) of 10 patients with multiple myeloma and in 3 of 4 patients it was associated with renal failure.

A total of 10 patients had renal failure in our study. Two patients of acute myeloid leukemia, 1 patients of acute lymphoblastic leukemia, 1 patient of Hodgkin's lymphoma and 4 patients of multiple myeloma were azotemic in the present study. Merrill D and Jackson H JR in 1943 (18) reported 2 cases of myelogenous leukemia associated with renal failure. In these, autopsy findings supported microvascular insufficiency from stasis and obstruction of blood vessels and glomeruli by masses of leukemic cells.

One of our acute lymphoblastic leukemia (ALL-L3 FAB) patient had hyperuricemic renal failure due to Grade '0' spontaneous tumor lysis syndrome, and precipitated by dehydration. Obrador GT et al in 1997 (19) reported a case who presented with acute renal failure secondary to massive lymphomatous infiltration of kidneys in whom chemotheraphy resulted in rapid improvement in renal function and regression of renal size. Gross hematuria from hemorrhagic necrosis of the kidney and tumor lysis syndrome from steroid induced lympholysis was additional features of this case.

Of the 60 patients, a total of 8 (13.33%) patients had hypercalcemia which included 3 (30%) patients of myeloma, 3 (8.33%) patients of leukemia, and 2 (14.28%) patients of lymphoma. This study closely correlates with the study of Burt ME and Brennan MF, 1980 (20) who reported the incidence of hypercalcemia in haematological malignancies as 10.9% and relatively high incidence was found in multiple myeloma (28.1%) followed by non- Hodgkin's lymphoma (13.0), leukemia (11.5%) and Hodgkin's disease (5.4%).

Two (22.22%) patients of non- Hodgkin's lymphoma in our study had calcitriol-mediated hypercalcemia. Baechler R et al in 1985 (21) reported that incidence of hypercalcemia in high and intermediate grade non-Hodgkin's lymphoma may be as high as 30%. This correlates well with our study.

In the present study, 3 (37.5%) of 8 hypercalcemic patients were in leukemic group and the hypercalcemia in them was related to parathyroid hormone related peptide. This closely correlates with the study of Ratcliffe WA et al, 1992 (22) who reported that 33% of the hypercalcemic patients in haematological malignancies were related to production of parathyroid hormone related peptide.

In our study, a total of 8 (13.33%) patients had hypocalcemia. Two (14.29%) patients of lymphoma and 6 (16.66%) of leukemia group had hypocalcemia while none of our multiple myeloma patients had hypocalcemia.

Mckee L.C. JR in 1975 (23) reported hypocalcemia in 19 (10.4%) of the 182 patients of leukemia group. This

was observed in 5 (9%) patients with acute leukemias, 5 (6%) patients with chronic lymphatic leukemia and in 9 (22%) patients with chronic myeloid leukemia. In 15 out of 19 cases hypocalcemia were related to poor renal function or to hypoalbuminemia.

Out of 26 acute leukemic patients, a total of 10(38.46%) including 6(40%) of acute myeloid leukemia patients and 4(36.36%) of acute lymphatic leukemia patients had hypokalemia. This study closely correlates with the recent observations in a review article by Filippatos TD et al, 2005 (24) who reported hypokalemia in 43-64% of acute leukemic patients.

In 10 (38.46) of our hypokalemic patients in acute leukemia group majority had it related to inappropriate kaliuresis, either due to lysozymuria-induced tubular injury or some leukemic factor induced renal potassium wasting. (25). One of our patients in chronic myeloid leukemia and 1 more in non-Hodgkin's lymphoma group had hypokalemia related to inappropriate kaliuresis. This increased urinary potassium loss could be due to hypercalcemia induced tubular damage, which might impair sodium reabsorption and lead to increased flow of sodium and water to the collecting tubules and subsequent potassium wasting (26).

A total of 7 (11.67%) i.e 2 (14.29) in leukemia, 2 (5.55) in lymphoma, and 3 (30%) in myeloma group had hyperkalemia. In 4 (57.14) of these patients hyperkalemia was related to renal failure while as 3(42.86%) others had hyperkalemia related to tumor lysis syndrome and associated urate nephropathy. Hyperkalemia could be due to the accumulation of electrolytes as a result of urate nephropathy or as a result of renal failure due to leukemic infiltration of the kidneys and/or severe leukostasis with consequent microvascular insufficiency(27). Furthermore, hyperkalemia could be the result of potassium release from malignant cells following cytotoxic therapy due to tumor-lysis syndrome which typically occurs in patients with lympho proliferative malignancies who are exposed to chemotherapy, radiation or corticosteroids but can occur spontaneously in the absence of treatment (28)

We reported hypophosphatemia in 11(18.33%) patients in this study . Out of these, 2 had lymphoma, 8 had leukemia and 1 more had multiple myeloma. Hypophosphatemia is a relatively common disturbance in patients with acute leukemias. Low serum phosphate levels have been reported in upto 30% of patients (29) .Young IS et al 1993 (30) described a case of severe hypophosphatemia due to both increased utilization of phosphate by rapidly growing tumor cells as well as tubular defect-associated excessive phosphate urinary losses.

In our study only 1 patient had hyperphosphatemia that too was in multiple myeloma group. This patient of multiple myeloma had treatment induced tumor lysis syndrome

In this study, a total of 4(6.67%) had hypouricemia. Three of the hypouricemic patients were in leukemic group and 1 more in lymphoma group.

Out of 60 patients, 9 (15%) had hyperuricemia which comprised 5 (13.89%) patients of lymphoma, 4 (11.11%) patients of leukemia and 1(10%) patient of multiple myeloma. Hyperuricemia resulting in acute uric acid nephropathy is the most frequently recognized metabolic cause of renal insufficiency in acute tumor lysis syndrome (31). Hyperuricemic acute renal failure is usually a complication of high turnover tumors (spontaneous tumor lysis syndrome) or of their successful treatment with rapid tumor lysis (frequently complicated by hyperphosphatemia and hyperkalemia) (32).

Seven (11.67%) of the 60 patients in our study had hyponatremia, 2 (14.29) of 14 patients of lymphoma, 4 (11.11%) of 36 patients of leukemia and 1 (10%) of 10 patients of multiple myeloma had hyponatremia. Three of our hyponatremic patients had it due to hypovolemic hyponatremia (gastrointestinal losses) and 1 more had it related to diuretic use. Whereas 2 other fulfilled the criteria for syndrome of inappropriate secretion of antidiuretic hormone (cytotoxic drugs related) and 1 more had inappropriate natriuresis probably due to leukemia induced tubular defect.Our study closely correlates with the study of Milionis HJ et al, 2005 (29) who reported hyponatremia in about 10% of their acute leukemia patients.

We found acid-base disturbance in 20(33.33%) patients among which 6(10%) had metabolic acidosis, 9(15%) alkalosis and the rest 5(8.33%) patients had mixed acid-base disturbance. Metabolic alkalosis in our 7 patients was probably related to hypercalcemia, volume depletion and hypokalemia while as respiratory alkalosis in 2 patients was related to respiratory tract infection and hypoxemia. Metabolic acidosis however was related to renal failure. Filippatos TD in 2005 (24) reported metabolic alkalosis in 35%, metabolic acidosis in 10% and mixed acid-base disturbance in about 15% of the acute leukemic patients.

In the present study 1 patient of multiple myeloma had treatment induced tumor lysis syndrome while 2 other patients (1 of ALL-L3 and 2nd in non-Hodgkin's lymphoma) had grade 'o' spontaneous tumor lysis syndrome as per Cairo-Bishop grading classification of tumor lysis syndrome (33)

CONCLUSION

In our study we found that majority of patients with haematological neoplasia had evidence of tumoral infiltration of Kidneys and metabolic derangements, which

needed timely intervention to improve the survival and prognosis in these patients.

Since these renal complications, whether tumor or treatment related, are often preventable and reversible, hence much can be done for these patients to improve their survival by decreasing or preventing these complications from occurring.

Renal involvement by tumor, although rare can sometimes be the sole manifestation of a haematological malignancy before it is detectable by routine methods. It can present as renal enlargement, obstructive uropathy, glomernlonephritis, tubular abnormalities or as paraneoplastic syndromes, so by keeping knowledge of these possibilities these tumor related catastrophes can be prevented from occurring or halted before these can endanger the life.

Abbreviations:

FAB: french American britain

Dam: diacetylmonoxime

$FENa^{+}$: fractional excretion of sodium

FEK^{+}: fractional excretion of potassium

$FEPo_4^{3-}$: fractional excretion of phosphorus

USG : ultrasonography

MHZ: megahertz

NSAIDS: non steroidal anti inflammatory drugs

NHL: non hodgkins lymphoma

CML: chronic myeloid leukemia

AML: acute myeloid leukemia

ALL: acute lymphocytic leukemia

CLL: chronic lymphocytic leukemia

GMC: government medical college

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