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Pattern of Haematological Disorders in a Tertiary Diabetic Hospital: A Pilot Study

DT FARHANA[a] , N QUAMRUN[b], C SUBHAGATA[c]

Summary:

Background: Patients with diabetes mellitus may suffer from various haematological diseases. A one year prospective study from July 2007 to July 2008 was done in the Department of Transfusion Medicine of BIRDEM to see the distribution of haematological diseases among the referred patients.

Objective: The aim of the study was to observe the pattern of hematological diseases in patients with diabetes mellitus.

Materials and Method: A total number of 111 new cases suffering from various haematological disorders were included in this observational study for one year duration from July 2007 to July 2008. Patients were diagnosed by peripheral blood film, complete blood count, bone marrow, hemoglobin electrophoresis. History of the patients including clinical informations were recorded with written consent from their very first arrival.

Results: Among the studied 111 patients, 23 (20.72 %) were suffering from various types of haemoglobinopathies and 88 (79.28 %) with other haematological diseases. When glycemic status was considered 65 (58.56%) patients out of 111 showed diabetes mellitus along with haematological diseases. Among those diabetic patients 11% had haemoglobinopathies, 25% had bleeding disorders, autoimmune diseases and marrow aplasia, 27% suffered from deficiency anaemia, anaemia of chronic diseases and haemochromatosis , where as 37% had various clonal haematological malignancy. Among haemoglobinopathies group, beta thalassaemia major was 21.74%, beta thalassaemia trait 47.83%, haemoglobin E-trait 17.39% and haemoglobin E-disease was 13.04%. Out of 23 Haemoglobinopathy patients 14 (60.87%) were male and 9 (39.13%) were female. Out of 88 patients with other haematological diseases except haemoglobinopathy 26 (29.54%) were of various haematological malignancies, 16 (18.18%) were of bleeding disorders, autoimmune diseases and marrow aplasia and 47 (53.41%) out of 88 patients had deficiency anaemia, anaemia of chronic diseases and haemochromatosis. In this group 40 patients (45%) were male and 48 (55%) patients were female.

Conclusion: This study shows majority patients with haematological diseases were suffering from diabetes mellitus. Among the haemoglobinopathies group, male were predominant and among the other haematological diseases except haemoglobinopathies group, female were predominant. From this study we suggest further multicentred study to see any precipitating cause between haematological diseases and diabetes mellitus. There is also an immense need to maintain registry of haematological diseases with a plan to establish state of art haematology services in all tertiary specialized hospitals including BIRDEM.

Key words: haemoglobinopathy, clonal hematological malignancies, anaemia, bleeding disorder, diabetes mellitus, cancer

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Introduction

The growing problem of haematological diseases & diabetes mellitus are indicative of globally increasing trend of non-communicable diseases. Diabetes and cancer are two conditions that individually overwhelm both patients and clinicians. Approximately 8-18% of people with cancer have diabetes[1]. Patients with diabetes and cancer have poorer prognosis compared with those without diabetes[2]. Diabetes and hyperglycaemia are associated with higher infection rates, shorter remission period and shorter median survival times as well as higher mortality rates[2-6]. Researchers hypothesize that exposure to hyperglycaemia, elevated insulin concentrations and the growth-promoting effects may stimulate the development of progression of cancer[2]. In haematological malignancy normal bone marrow haemopoiesis is

a. Dipta Tashmim Farhana, FCPS (Haematology), MTM (Transfusion Medicine), Assistant Professor & Head, Transfusion Medicine Department, BIRDEM.

b. Quamrun Nahar, PhD, Senior Research officer, Department of Biochemistry and Cell Biology, BIRDEM.

3 Subhagata Choudhury, FCPS, M.Phil, Director Laboratory Services, BIRDEM.

Address of Correspondence: Dr. Tashmim Farhana Dipta, FCPS (Haematology), MTM (Transfusion Medicine), Assistant Professor & Head Transfusion Medicine Department, BIRDEM and Ibrahim Medical College, Phone: 01817049343, e-mail: tashmim@yahoo.com

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often disrupted due to infiltration of clonal tumor cell growth[7]. The treatment and therapies for diabetes in the setting of cancer present a major challenge for clinicians[2]. Haematological malignancies constitute approximately 7% of all cancer cases in Sweden and leukaemia in that country is the most common malignancy among children[7]. Study shows that approximately 150 million people have diabetes mellitus world wide and this may double by 2025[8], where as the role of diabetes as a risk factor for cancer is still uncertain[9].Various study shows there is an increased risk for development of cancer among diabetes[6,10] and vice versa [11]. Cancer is the second most killer in the world after cardio-vascular diseases[12]. About 13% of all death in the world is currently caused by cancer; where as in 2007 about 6% patient suffering from diabetes which is growing as a silent killer[12]. Study shows there is an association of abnormal glucose metabolism, higher body mass index and risk of haemopoietic cancer like leukaemia, multiple myeloma[11].Previous study suggested that, diabetes mellitus a frequent cause of renal insufficiency[13] also causes more activation of prothrombotic markers in acute myeloid leukaemia or disseminated intravascular coagulation[14]. In acute lymphoblastic leukaemia secondary to chemotherapy, transient hyperglycaemia develop due to consequence of insulin resistance, induced by glucocorticoid , as well as, due to decrease insulin synthesis by L-asparaginase[15-17] and occurs in 4.4 % of patients with acute lymphoblastic leukaemia[16]; whereas, episode of infection is more in other leukaemia[18,19]. On the other hand, iron deficiency is the most common cause of anaemia affecting about 500 million people[20]. Study shows iron deficiency anaemia and anaemia of chronic disease are common in diabetic patients[20] and is associated with increased morbidity, mortality and poorer prognosis in diabetic-associated co morbid conditions[18-20]. Diabetes occurs in hereditary haemochromatosis and transfusional haemosiderosis due to insulin deficiency, resistance[21] and excessive iron deposition[22-24]. Study shows using iron chelating agent [21, 25] and blood donation [21, 25] decrease development of diabetes in such patients. Where as, chronic autoimmunity is associated with autoimmune haemolytic anaemia, idiopathic thrombocytopenic purpura [26, 27]and obesity[26-30] which increase the risk of myeloma among older and influences chronic myeloid leukaemia and Hodgkin's lymphoma [26-29]; all these show association with diabetes[26-30]. Persons with haematological malignancies such as leukaemia, lymphoma especially with extranodal lymphoma[33, 34]or myeloma and blood dyscrasias often have coexisting diabetes mellitus [26-34, 36]. Study shows chronic lymphocytic leukaemia , which is 20-30% of all leukaemia[32] and diabetes mellitus both causes suppression of immune system, hyperglycaemia and higher risk of infection among diabetic[18,19, 37].

In USA the most common haematological malignancy among the child up to 14 years is leukaemia[37]. In United States there is increasing trend of cancer and prevalence among female is 0.3% with non-Hodgkin's lymphoma is 4% and leukaemia is 3%[37]. Whereas, previous studies suggested that among haemoglobinopathies, prevalence of thalassemia is 16% in Cyprus, 3-14 % in Thailand, and 3-8 % in populations from India, Pakistan, Bangladesh and China [38-40]. A lower prevalence shown in Africa (0.9%) and northern Europe (0.1%) [38]. Worldwide, Hb E-beta-thalassemia is most frequent and the incidence of Hb- E approaches 60% of the populations in many regions of Southeast Asia[39]. As a growing global public health problem in the next 20 years an estimated 900,000 births of clinically significant thalassemic are expected to occur [39]. In Bangladesh a conservative World Health Organization (WHO) report estimates that, about 3.0% of populations are carriers of beta thalassemia and 4.0% are carriers of Hb-E[40].

There is dearth information regarding haematological disorders among the diabetic patients in Bangladesh. So this pilot study was designed to see the prevalence of diabetes mellitus and pattern of haematological diseases among patients attending BIRDEM (Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders).

Methodology:

In this observational study, one hundred and eleven patients between fifteen to ninety years of age, suffering from various haematological disorders reported academically in the Transfusion Medicine Department of BIRDEM as out patient or indoor

referral cases. Patients were diagnosed previously for various haematological diseases with modern equipments and special emphasis was given on peripheral blood film (Leishman's stain), complete blood count (automated cell counter: Sysmax XT-1800i, model Japan.), bone marrow (marrow puncture needle: Salah), haemoglobin electrophoresis (Sebia: France, Hydragel Heamoglobin –E: K-20) and coagulation profile (Prothrombin time: Start Diagnostic Stago, Activated Partial thromboplastine time: COAG-A-Mate XM) done in BIRDEM laboratory division and Haematology Department of BSMMU (Bangabandhu Seikh Mujib Medical University). Histories of the patients including clinical information's were recorded with written consent from their very first arrival. Only new cases were enrolled in this study, those were referred to the Department of Transfusion Medicine as a part of consultation from various out patient clinics and inpatient departments of BIRDEM. Study period was one year from July 2007 to July 2008. Data were analyzed using Microsoft office excel 2003 for Windows version.

Results:

Total number of 111 patients between fifteen to ninety years of age, suffering from various haematological disorders reported in the Transfusion Medicine Department of BIRDEM as out patient or indoor referral in BIRDEM. 65 patients out of 111 (58.56%) showed diabetes mellitus along with haematological diseases. That means majority patients showed diabetes mellitus along with benign or malignant haematological diseases. In the group of 88 patients (79.28%) with other haematological diseases except haemoglobinopathy 25% patients were of bleeding disorders, disseminated intravascular coagulation and autoimmune haemolytic anaemia had diabetes mellitus; 27% patients with deficiency anaemia, haemochromatosis and marrow aplasia had diabetes mellitus; where as 37% patients with clonal malignant haematological diseases were suffering from diabetes mellitus was shown in figure no-1. Among patient in this group, 30.68% which was majority (27 patients), were suffering from iron deficiency anaemia and next highest was 17.04% with anaemia of chronic diseases. Among them, 55% (48 patient) were female and 45% (40 patient) were

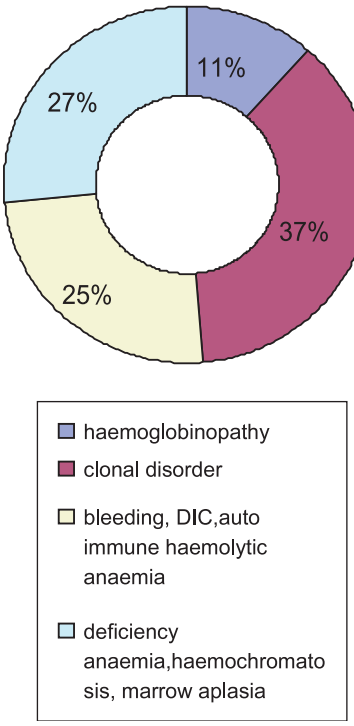

Fig.-1: *Shows distribution of patient with diabetes mellitus (N=65)*
11% in haemoglobinopathy group, 25% patients with bleeding disorders, disseminated intravascular coagulation and autoimmune haemolytic anaemia, 27% with deficiency anaemia,haemachromatosis and marrow aplasia patients and 37% patients with clonal malignant diseases were suffered from diabetes mellitus.

male, so female were higher in this group. According to the disease pattern male were predominantly suffering from anaemia of chronic disease, haemophilia, polycythaemia, megaloblastic anaemia, Hodgkin's and non-Hodgkin's lymphoma, haemochromatosis, acute myeloid leukaemia , acute lymphoblastic leukaemia and chronic myeloid leukaemia. Where as, in female, iron deficiency anaemia, autoimmune haemolytic anaemia, abnormal bleeding or disseminated intravascular coagulation, idiopathic thrombocytopenic purpura, multiple myeloma, chronic lymphocytic leukaemia, aplastic anaemia, myelodysplastic syndrome group were predominant. In this group of 88 patients, 26 (29.54%) patients were suffering from various clonal haematological malignancies eg. polycythaemia

rubra vera, Hodgkin's diseases, non-Hodgkin's lymphoma, multiple myeloma, acute myeloid leukaemia, acute lymphoblastic leukaemia, chronic myeloid leukaemia, chronic lymphoblastic leukaemia, myelodysplastic syndrome. 16 patients (18.18%) with bleeding disorders e.g. haemophilia, abnormal bleeding or disseminated intra vascular coagulation, autoimmune diseases, idiopathic thrombocytopenic purpura, aplastic anaemia or marrow aplasia and 47 (53.41%) patients were of deficiency anaemia e.g. iron deficiency anaemia, megaloblastic anaemia, anaemia of chronic diseases and haemochromatosis. Among 88 patients one female patient had both iron deficiency anaemia and multiple myeloma. All these three categories of patients were elaboratively distributed in figure no-2, 3 and 4 and total distributions of 88 patients according

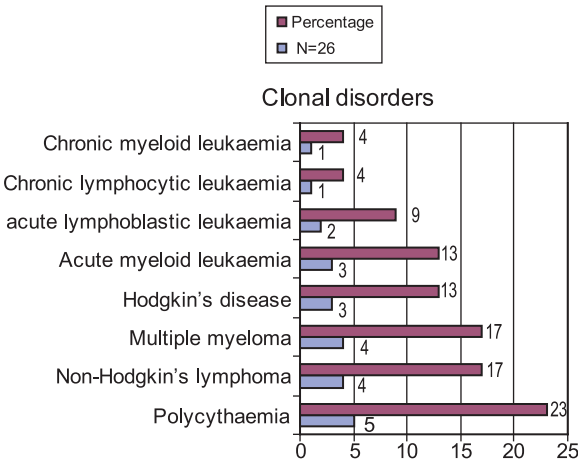

Fig.-2: *Distribution of clonal haematological malignancies only (N=26).*

to diseases were shown in table no-1. Highest age among these patients was in between 50-60 years of age group (21.59%) and next 20.45% were in between 60-70 years of age group. On the other hand, 23 patients out of 111(20.72 %) were suffering from various types of haemoglobinopathy. Among them beta thalassaemia major 21.74%, beta thalassaemia trait 47.83%, haemoglobin E-trait 17.39% and haemoglobin E-disease 13.04% were shown in table no-II. Out of 23 haemoglobinopathy patients, 14 (60.87%) were male and 9 (39.13%) were female. In this group male patients were predominantly suffering from haemoglobinopathies. Among these

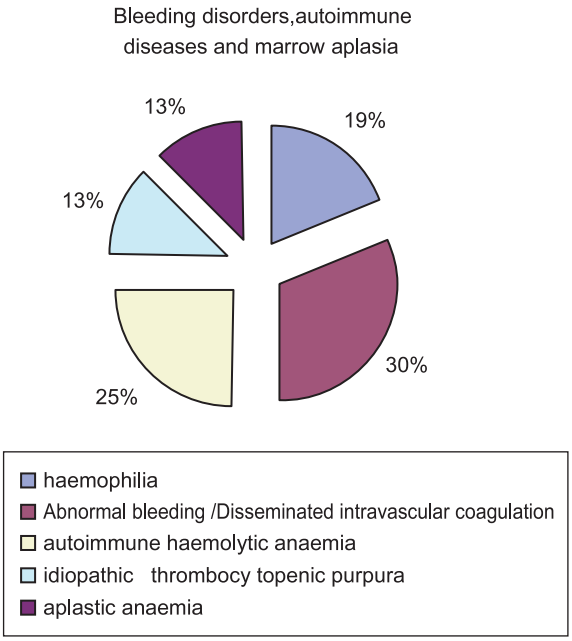

Fig-3: *Distribution of bleeding disorders, autoimmune diseases and marrow aplasia (N=16).*

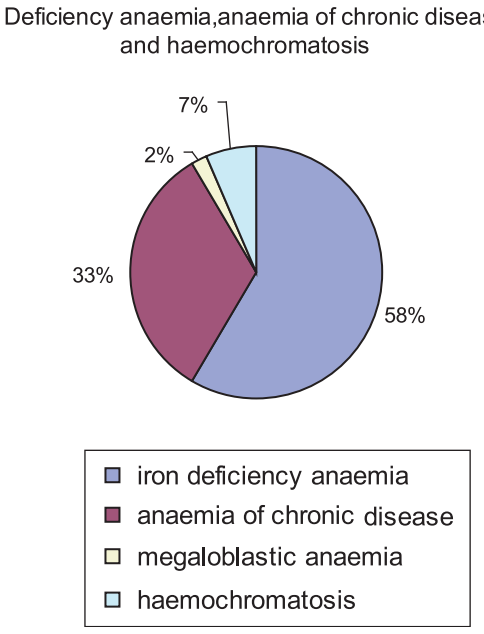

Fig.-4: *Distribution of deficiency anaemia, anaemia of chronic diseases and haemochromatosis(N=47).*

male patients 43% had beta thalassaemia trait , 29% had beta thalassaemia major, 21% were suffering from haemoglobin E trait and 7% had haemoglobin E diseases; where as among the female 56% had beta

thalassaemia trait, 22% had haemoglobin E diseases and 11% had either beta thalassaemia major or haemoglobin E trait. In case of age distribution highest number of patients with haemoglobinopathy was 60.87 % in 20-30 years of age group. In this group diabetes mellitus was 11%, shown in figure no-1. On the other hand, among total patients, 46 were non-diabetic. Among them 31(67%) were male and 15 (33%) were female.

Table-I

Distribution of other haematological diseases except haemoglobinopathy. (N=88)

Name of the disease		Number	Percentage
(i)	Iron deficiency anaemia	27	30.68
(ii)	Anaemia of chronic disease	15	17.04
(iii)	Primary polycythaemia	5	5.68
(iv)	Abnormal bleeding / Disseminated intravascular coagulation	5	5.68
(v)	Autoimmune haemolytic anaemia	4	4.54
(vi)	Non-Hodgkin's lymphoma	4	4.54
(vii)	Multiple myeloma	4	4.54
(viii)	Haemophilia	3	3.41
(ix)	Haemochromatosis	3	3.41
(x)	Hodgkin's disease	3	3.41
(xi)	Acute myeloid leukaemia	3	3.41
(xii)	Myelodysplastic syndrome	3	3.41
(xiii)	Acute lymphoblastic leukaemia	2	2.27
(xiv)	Aplastic anaemia	2	2.27
(xv)	Idiopathic thrombocytopenic purpura	2	2.27
(xvi)	Megaloblastic anaemia	1	1.14
(xvii)	Chronic lymphocytic leukaemia	1	1.14
(xviii)	Chronic myeloid leukaemia	1	1.14

Table.-II

Shows Haemoglobinopathies (N=23)

Types of Haemoglobinopathy	No of patients	Percentage
Beta thalassaemia trait	11	47.83
Beta thalassaemia major	5	21.74
Haemoglobin E-trait	4	17.39
haemoglobin E-disease	3	13.04

Discussion:

Cancer is the second most killer in the world after cardio-vascular diseases[12]. About 13% of all death in the world is currently cause by cancer[12].Where as in 2007 about 6% patient were suffering from diabetes mellitus which is growing as a silent killer[12]. When glycaemic status was considered 58.56% (65 patients) showed diabetes mellitus along with haematological diseases in our study. Thus our pilot study supports studies of different countries [2,6-10,16-19,20-24,26-31,35,37-40] and showed that, there is a correlation of diabetes mellitus with various haematological diseases[13-17,20-24]. Table No-1 shows the distribution of 88 patients with haematological diseases except haemoglobinopathy. Among these 88 patients distribution of diseases, age and gender has correlation with studies in different counties [6-20, 26-37]including Bangladesh[41, 42]. Figure-2 shows, 26 (29.54%) with various clonal haematological malignancies, Figure-3 shows 16 patients (18.18%) with bleeding disorders, autoimmune diseases and marrow aplasia and Figure-4 shows 47 (53.41%) out of 88 patients have deficiency anaemia, anaemia of chronic diseases and haemochromatosis .These results support studies in different countries[6-20, 26-37]. Our study also suggests that iron deficiency anaemia and anaemia of chronic diseases were common among diabetic patients, which supports studies in various countries [20]. This study supports the increasing trend of cancer in female reported in other study [37] including Bangladesh[42].Our Study also shows 37% diabetic had various clonal haematological malignancies[26-34, 36]. Figure no.1 shows the percentages of diabetic patients with both benign and malignant haematological diseases and supports other studies with leukaemia, lymphoma, myeloma and haemochromatosis along with diabetes mellitus [26-30, 31]. Association between lymphoid neoplasm, blood dyscrasias , bleeding disorders, marrow aplasia, auto immune diseases and diabetic mellitus support studies in different countries which also reflected in our study [30, 31, 35-37]. In our study majority patients show diabetes mellitus along with benign or malignant haematological diseases which support studies in different countries[13-16, 20-24, 26-29, 30-37]. Table No-2 shows distribution of 23 patients out of 111 (20.72 %) were suffered from various types of haemoglobinopathy and among them 14 (60.87%)

were male and 9 (39.13%) were female. In this study, age distribution of patient with haemoglobinopathy shows majority, that is, 60.87 % were in 20-30 years of age and were suffering from diabetes mellitus (11%), which supports the study showed insulin deficiency , insulin resistance and iron overload had strong correlation with haemoglobinopathy and diabetes mellitus [21-25]. Thus in distribution of diseases, age and gender our study supports studies in different countries [21-24, 38-40]. Our study showed 43% male had beta thalassaemia trait , 29% had beta thalassaemia major, 21% with haemoglobin E trait and 7% had haemoglobin E diseases; where as, 56% female had beta thalassaemia trait , 22% had haemoglobin E diseases and 11% had beta thalassaemia major or haemoglobin E trait and support other studies including Bangladesh [21-24, 38-40]. In this observational pilot study we observed that, diabetic patients with haematological diseases were anaemic and had more morbid state which show correlation with studies done in different countries[13, 1,4,21,22-25,27,29].This morbidity increases with chemotherapy which also correlates with other studies [31,32,35]. Thus our study supports studies done in Sweden[7], USA[11, 37], Bangladesh[41-43] and other studies[2, 6, 10, 13-17, 20-24, 26-40].

Conclusion:

This pilot study shows majority of benign and malignant haematological patients were suffering from diabetes mellitus. According to this study haematological diseases and malignancy except haemoglobinopthy, were predominant in female patients; where as, haemoglobinopthies were more in male group. So there is a need of further elaborative study to see if there any precipitating cause in patients suffering from diabetes mellitus with haematological diseases. There is also an immense need to maintain registry of these patients with a plan to establish state of art Haematology Department in all tertiary specialized hospitals including BIRDEM.

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