



Volume: 3 - Issue 2
July to December 2020

ISSN NO : 2709-2577 (Online)

ISSN NO : 2709-2569 (Print)



JOURNAL
OF INDUS MEDICAL COLLEGE
(JIMC)

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EDITORIAL**COVID-19 INFECTION AND RISK OF THROMBOEMBOLISM**

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Editorial received on: 09-07-2020

Editorial accepted on: 24-12-2020

COVID-19 has emerged from China and spread throughout globe since December 2019. The causative pathogen is recognized as novel enveloped RNA beta-coronavirus, ⁽¹⁾ having similar genetic structure to SARS-CoV, and named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has now been declared as public health emergency by World Health Organization (WHO). ⁽²⁾

Millions of casualties, morbidities and mortalities have been reported worldwide, with number going on. ⁽³⁻⁴⁾ The clinical history of the disease is heterogeneous and ranges from mild non-specific symptoms (e.g. dry cough, fever and diarrhoea etc) to lung insufficiency, severe pneumonia and death. In case of lung insufficiency, mechanical ventilation is required or individuals with multiple organ failure, treatment is according to underlying conditions and age. ⁽⁵⁾ Pro-inflammatory markers are usually associated with the severity of disease including interleukin-2, interleukin-6, interleukin-7, interleukin-10, interferon γ -induced protein-10, granulocyte colony-stimulating factor, macrophage inflammatory protein-1A, monocyte chemoattractant protein-1 and tumour necrosis factor- α ; though the reason behind this cytokine storm is still not clear. ⁽⁶⁾ Among various biochemical and clinical parameters which are linked with poor prognosis of the disease, a D-dimer level in high range is

good predictor for the development of acute respiratory distress syndrome (ARDS). In Tongji Hospital, Wuhan, China, Tang et al evaluated prognosis of 183 patients with confirmed 2019-nCoV pneumonia. He showed that in patients with COVID-19, disseminated intravascular coagulation (DIC) is frequent cause of disease worsening. Abnormalities of coagulation and increased level of D-dimer were significantly associated with high mortality and co-morbid complications of thromboembolism. The disease was more severe in patients with severe lung failure. ⁽⁷⁾ Cui et al evaluated 81 patients admitted to ICUs, and described the thromboembolism prevalence rate of about 25%. ⁽⁸⁾ Unfractionated heparin (UFH) and low molecular weight heparin (LMWH) can reduce the mortality rate in severe patients of COVID-19 if started at prophylaxis dose, ⁽⁹⁾ reflecting a score for sepsis-induced coagulopathy (SIC) of ≥ 4 (40% Vs. 64.2% with p-value of 0.029) or level of D-dimer six times higher as compared to

Article Citation:

Naz L, covid-19 infection and risk of thromboembolism. JIMC. 2020; 3(2): 1-2

normal (32.8% Vs. 52.4% with p-value of 0.017). In affected Italian patients in intensive care unit, frequency of thromboembolic complications is higher (up to 30%). Though, the incidence of deep venous thrombosis in Italian patients without COVID-19 was 0.025%.⁽¹⁰⁾ Median age of included patients was 45.4 years, which may be contributing factors for increased frequency of thromboembolic complications, in contrast to Chinese population with median age of 37.4 years.⁽⁴⁻⁵⁾ Major thromboembolic complications in Italian patients were pulmonary embolism and venous thromboembolism; all documented by CT scan or compressive ultrasonography.

Almost all patients show variations in parameters of haemostasis including: 1) Increased D-dimer levels (>1,000 at the time of admission, and rapidly rise thereafter); 2) Increased fibrinogen that may be utilized in later stages of disease; 3) Decreased platelet count (thrombocytopenia) but less incidence than disseminated intravascular coagulation; and 4) Normal or sometimes increased partial thromboplastin time (PTT) and international normalized ratio (INR). Other coagulation tests show increased von Willebrand factor levels, increased factor VIII levels, and normal protein C, S and antithrombin III levels. Data from COVID-19 patients in ICU is summarized in Table 1.

Table 1: Coagulation Profile in COVID-19 DIC, Acute DIC and Chronic DIC

Parameters	COVID-19 Disseminated Intravascular Coagulation (DIC)	Acute (decompensated) Disseminated Intravascular Coagulations (DIC)	Chronic (compensated) Disseminated Intravascular Coagulation
Platelet count	Normal/Decreased	Decreased	Variable
Prothrombin time (PT)	Normal/Prolonged	Prolonged	Normal
Partial thromboplastin time (PTT)	Normal/ prolonged	Prolonged	Normal
Thrombin time (TT)	Normal/prolonged	Prolonged	Normal/slightly prolonged
Plasma fibrinogen	Increased	Decreased	Normal/increased
Plasma factor VIII	Increased	Decreased	Normal
Fibrin degradation products (FDPs)	Increased	Increased	Increased
D-dimer	Increased	Increased	Increased

Disseminated intravascular coagulation (DIC) in patients with COVID-19 is a kind that is recognized by hypercoagulability. Yet exact mechanism for DIC in COVID-19 is not clear; though release of cytokine and inflammatory drive may be the contributing factors in impairment of coagulation that lead to thromboembolic complications. Stimulation of interleukin-6 (IL-6) may up-regulate synthesis of fibrinogen by liver and virus may combine directly to endothelial cells and causes damage to alveoli.

Disseminated intravascular coagulation (DIC) seems to be the indicator for severity of disease and associated with poor clinical outcome.⁽⁷⁾ From 40 autopsies, $\frac{1}{4}$ showed macrothrombosis with classical pulmonary embolism pattern. More than $\frac{2}{3}$ demonstrated thrombi in microvessels, related to diffuse damage of alveoli and interstitial lung infiltrates of macrophages, granulocytes and giant platelets. These are in agreement with study by Luo et al. (11) These findings postulate the mechanism of inflammatory-mediated micro- and macrothrombosis as classical process of damage in COVID-19 severe patients. Improving patient outcome in COVID-19 by different simple and cheap antithrombotic agents is tempting, but to adapt aggressive approach, various factors should be clarified and addressed, especially to define suitable timing to start treatment and dosage that may influence concomitant drug therapies.

Scientific community is working for more strong evidence on role of anti-platelet therapy or heparin in COVID-19-associated coagulopathies, the Italian Society on Thrombosis and Hemostasis published some recommendations, (12) for the management of COVID - 19 - associated coagulopathies (Figure 1-3). 1) Evaluation of individual risk along with laboratory investigations must include function of hemostatis, platelet count

and D-dimer; ultrasound screening for deep venous thrombosis (DVT). 2) Treatment with UFH, LMWH or fondaparinux at specified doses indicated for VTE prophylaxis is recommended in all hospitalized COVID-19 patients; patients with contraindications to anticoagulant therapy should be managed with limb compression. Throughout stay at the hospital, thromboprophylaxis should be given, followed by maintenance at home for 1-2 weeks after discharge from hospital. 3) Treatment with intermediate dose LMWH (e.g. enoxaparin 4,000 IU S/C every 12 hours) can be given in patients with multiple risk factors for VTE (e.g. BMI>30, active malignancy or previous VTE etc). In patients with renal failure, activated Xa should be strictly monitored. 4) LMWH or UFH therapeutic doses are not appreciated without evident VTE diagnosis or as bridging strategy in individuals on vitamin K antagonists; though cannot be recommended in all COVID-19 infected patients. 5) Caution should be taken for direct oral anticoagulants and vitamin K antagonists due to interaction with antiviral mediations. 6) Strong cooperation between specialists of various specialities should be made for multi-disciplinary approach in COVID-19 patients.

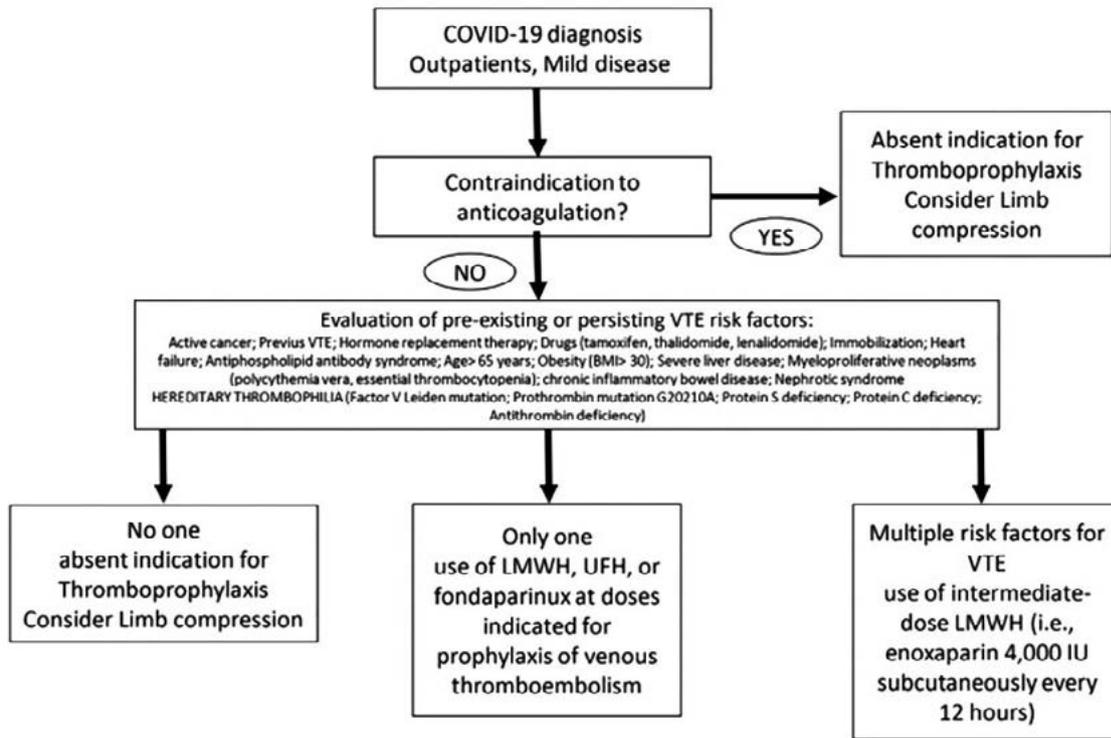


Figure 1: Prophylaxis of Venous Thromboembolism Therapy Scheme for COVID-19 Diagnosed Patients with Mild Disease (adapted from Italian Society of Thrombosis and Hemostasis)

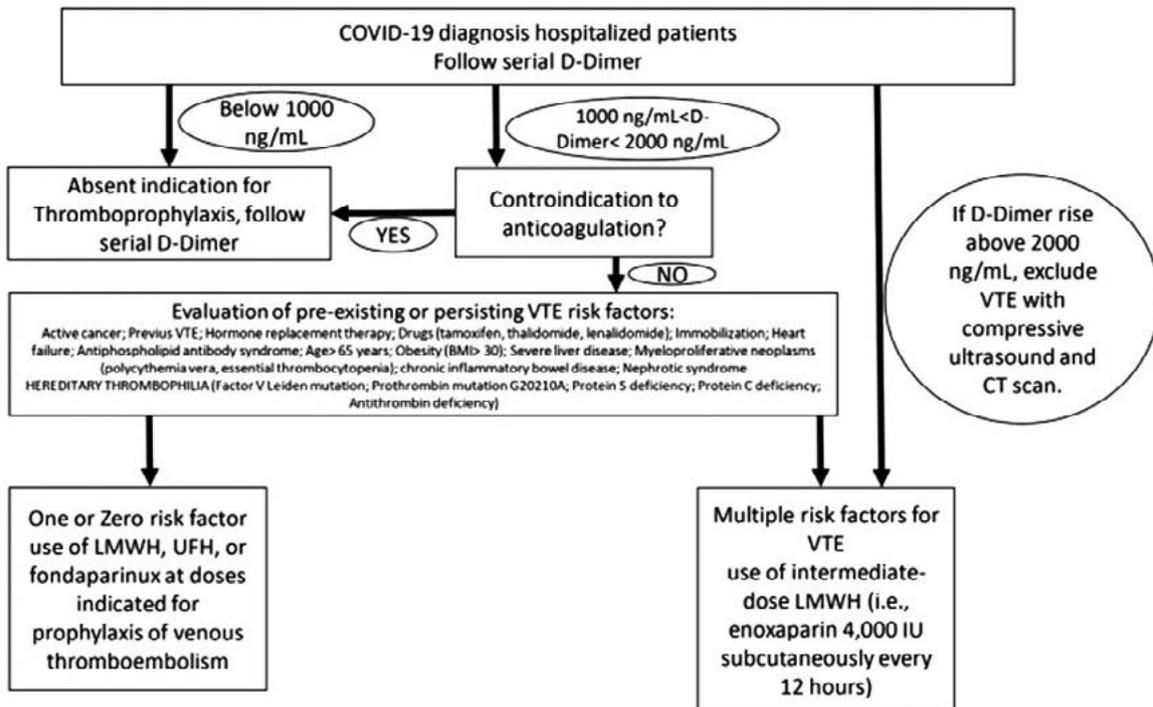


Figure 2: Prophylaxis of Venous Thromboembolism Therapy Scheme for COVID-19 Hospitalized Patients (adapted from Italian Society of Thrombosis and Hemostasis)

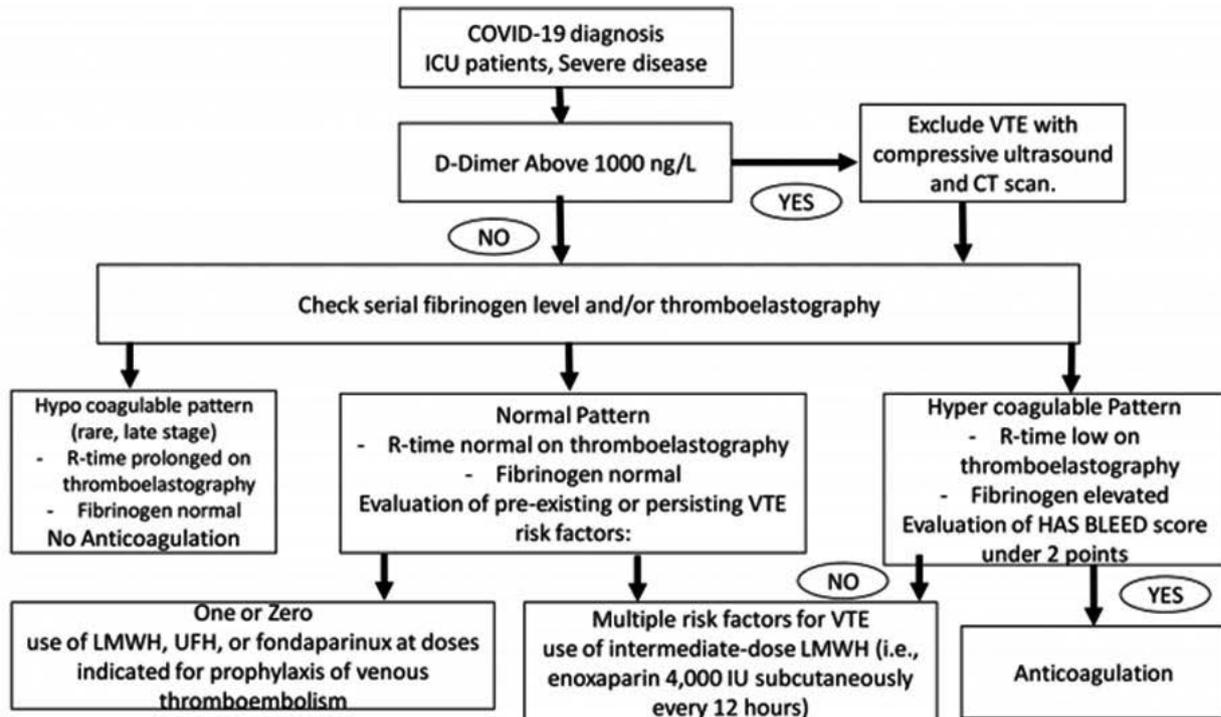


Figure 3: Prophylaxis of Venous Thromboembolism Therapy Scheme for COVID-19 ICU Patients (adapted from Italian Society of Thrombosis and Hemostasis)

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

LN - Manuscript Writing

ORIGINAL ARTICLE**HEMATOLOGICAL AND BIOCHEMICAL PROFILE OF PATIENTS WITH MACROCYTIC ANEMIA AT TERTIARY CARE HOSPITAL**¹Lubna Naz, ¹Muhammad Wasif Saleem¹Department of Pathology, Chandka Medical College, SMBBMU Larkana**Corresponding Author:**

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Article received on: 22-07-2020**Article accepted on:** 09-12-2020**ABSTRACT****BACKGROUND:**

Anemia is a global nutritional problem, and the risk of morbidity and death is higher in all age groups. Macrocytic anemia is usually caused by abnormalities that affect the maturation of erythroid precursors in the bone marrow. Because the clinical manifestations of different types of anemia are similar, hematological parameters (such as hemoglobin, red blood cell count, and peripheral blood smear) can be used to diagnose anemia.

MATERIALS AND METHODS: This is a cross-sectional study conducted in the Department of Pathology, Chandka Medical College Hospital, Larkana for a period of 6 months (January 2020 to June 2020). A total of 54 patients with low hemoglobin levels between 15 and 65 years old were selected, and venous blood samples with an MCV > 100 fL were selected as the study subjects.

RESULTS: The study included 54 patients with macrocytic anemia, with an average age of 32.88 ± 11.38 years old, and women were dominant group. The hemoglobin level of men was slightly lower than that of women. The red blood cell count of men was slightly higher.

There was a significant difference between male and female serum vitamin B12 and folic acid.

CONCLUSION:

The hemoglobin, red blood cell count, percentage of reticulocytes and peripheral blood smear are important parameters for the diagnosis of certain types of anemia. Evaluation of serum folate and vitamin B₁₂ levels and other hematological parameters is important for the diagnosis of macrocytic anemia and its correlation.

KEYWORDS: Macrocytic anemia, hematological, biochemical, vitamin B₁₂, folate.

Article Citation:

Naz L, Saleem WM, hematological and biochemical profile of patients with macrocytic anemia at tertiary care hospital. JIMC. 2020; 3(2): 7-12

INTRODUCTION

Anemia is a global nutritional problem that affects nearly 2 billion young people, adolescents and pregnant women at risk of morbidity and death.¹⁻² In general; the disease is connected with decreased production/increased destruction of red blood cells. The concentration of blood (RBC) or hemoglobin (Hb) affects oxygen circulation, which in turn affects maternal, and childbirth outcomes, optimal growth of children, poor learning, and decreased productivity and output during childhood.³⁻⁴ Diet, irregular eating habits and physical conditions (such as pregnancy) are risk factors for anemia in adolescents.⁵⁻⁶

According to data from the World Health Organization (WHO), the hemoglobin concentration of men less than 13 g/dl, 12 g/dl for non-pregnant women, 11 g/dl for pregnant women, and 12 g/dl for children 14 years old, ⁵ 11 g/dl for children up to 11 years old and 11 g/dl for children under 5 years are the diagnostic criteria for anemia.⁷ One of the basis for the classification of anemia is based on this basic mechanism including low productivity, increased destruction and massive blood loss. The second method classifies anemia based on changes in red blood cell morphology, and is usually related to the cause of red blood cell deficiency. The shape of red blood cell deficiency is classified into normal, small cell or large cell morphology.⁸

According to its size, when the average cell volume (MCV) > 100 fL, red blood cells are called ovalocytes. This is a characteristic of macrocytic anemia and is usually caused by an abnormality that alters the maturation of erythroid precursors in the bone marrow.^{4,9} Megaloblastic anemia is the most common cause of macrocytic anemia. The coenzymes required for thymine and purine synthesis are almost free of vitamin B12 and folic acid,

which can lead to impaired DNA synthesis, ineffective erythropoiesis and intramedullary hemolysis.¹⁰⁻¹¹

Because the clinical symptoms of different types of anemia are similar, the differential diagnosis of macrocytic anemia can be made by physical examination, hematological parameters such as hemoglobin, red blood cell markers such as mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), and with a peripheral blood smear, the main aim of which was to assess the hematological and biochemical parameters in a patients with macrocytic anemia.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Pathology Department Chandka Medical College Hospital, Larkana between January 2020 to June 2020. Before the sample preparation, a total of 54 patients aged 15 to 65 years with low hemoglobin were examined for the diagnosis of anemia according to WHO criteria and MCV > 100 fL. Samples were collected using EDTA-containing tube and were immediately analyzed on Automated Hematology Analyzer Mindray BC-5000. The parameters assessed included hemoglobin, MCV, MCH, MCHC, reticulocyte count, and peripheral blood smear to diagnose anemia according to the WHO.⁷

The reference intervals for RBC indices were:

MCV: 80-100 fL, MCH: 27-32 pg, MCHC: 32-36 gm/dl, Reticulocytes: (Adults = 0.5%-2.5% and Infants = 0.5%-7%)

When MCV was more than 100 fL, anemia was reported as macrocytic.

Peripheral Smear Examination

For the peripheral blood examination, EDTA blood smears were taken and allowed to air dry, and then 0.25% Wright stain was poured over the entire slide and allowed to stand for

2-3 minutes, followed by an equal volume of distilled water. The tiny slides were washed thoroughly, dried, and examined under a light microscope. Peripheral smear examination findings such as macrocytic or normocytic cells, hyper-segmented neutrophils, polychromatic cells, basophils, tear cells, etc. were reported.

Reticulocyte Count

Equal volumes of EDTA patient blood and the new methylene blue reagent were mixed in a tube and incubated for 10 minutes at 37°C., after which a swab was taken and analyzed by immersion oil.

Analysis of Biochemical Parameters

For vitamin B₁₂ and serum folate analysis, venous blood samples were collected in gel vials, centrifuged for 10 minutes at 3500 rpm and then evaluated in a fully automated Mindray CL1000i Immunoassay.

Reference interval for Vitamin B₁₂ = 211-911 pg/ml

Reference interval for Folic acid = 3.56 – 20.0 ng/ml

Data Analysis

Gender, age, hemoglobin concentration, MCV, MCH, MCHC, percentage reticulocytes and other parameters were determined, serum vitamin B₁₂ and folic acid were analyzed and the data obtained were analyzed in SPSS 24.0.

RESULTS

Our study included a total of 54 patients with macrocytic anemia aged 15 to 65 years with a mean age of 32.88 ± 11.38 years, including 20 males and 34 females with male: female ratio 1:2. Figure 1 shows the age distribution of male and female patients with macrocytic anemia. In the age group > 60 years, the distribution of the hemoglobin and erythrocyte indices by age was compared, and it was found that

in the age group 45-60 years, the hemoglobin level exceeds 8 g/dL, which is more than that of other patients. Levels of hemoglobin according to age groups are summarized in tables 2 and 3. In the peripheral blood smear findings, of 54 cases, 41 cases were identified as macrocytic anemia and 13 cases normocytic anemia. This macrocytic and normocytic anemia was demonstrated with additional features such as hyper-segmented neutrophils, polychromatic cells, basophilic stippling, and tear cells. Total serum levels of vitamin B12 and folic acid have been shown to be decreased in patients with macrocytic anemia. It was also found that the serum levels of these markers are significantly different in patients with male and female anemia (p<0.05).

DISCUSSION

First, vitamin B₁₂ and folic acid deficiencies are the most likely cause of macrocytosis (MCV>100 fl), which leads to macrocytic anemia. In some cases, however, the cause remains unclear. However, anemia with normal MCV may indicate a chronic or mixed type of anemia. In this study, we used a hematological findings, peripheral blood smear examination findings and biochemical findings to identify macrocytic anemia and correlated the results with their gender and age group.

In our study, the highest incidence of macrocytic anemia was observed in females as compared to male in the maximum age group of 18 to 25 years while Banjare B et al., Deepankaret et al. and Iqbal S et al. observed the higher incidence of macrocytic anemia in men than in women.^{2,13-14} A study by Rayamajhi et al. showed higher incidence in age group of 15-30 years.⁵ A similar age distribution was also found by Unnikrishanan et al. and Deepankar et al. with a mean age of 35.7 ± 16.1 years and 39 years.06 ± 8.9 years respectively.¹²⁻¹³

In the distribution of hemoglobin by age,

patients aged 18 to 25 years had the lowest hemoglobin level of 7.19 ± 1.81 , while patients aged 46 to 60 years had the highest hemoglobin level. An increase in MCV was observed in all cases. The largest red blood cell size was found in patients under 18 years of age (109.36 ± 5.11 fl) and the smallest in patients over 60 years of age (104.41 ± 3.74 fl). In most cases, the MCH value was increased, with a higher incidence in the age group 36-45 and less at the age of 46-60 years. Similarly, the maximum number of reticulocytes was found in the age group 18-25 while at least in people over 60.

In comparison to our study, Pudasaini S et al. observed that people with low MCH observed low MCHC levels and low MCH and MCHC levels in children aged 12-14 years.¹⁵⁻¹⁶ Anemia, low RBC counts were due to premature destruction of RBCs, and anemic patients had low PCV levels but elevated MCV, MCH, and MCHC levels, which fit well into this study. Kannan A et al. also showed other causes including leukemia, multiple myeloma and myelofibrosis etc. There was a significant difference in MCV between megaloblastic and non-megaloblastic macrocytosis.¹⁷

In this study, out of 54 cases, 40 showed both decreased levels of folate and vitamin B₁₂ and also the distinction between males and females were found to be statistically significant ($p < 0.05$). In distinction to our findings, Iqbal SP et al pointed out of 220 pernicious anemic patients, 71% of folic acid deficient patients had vitamin B₁₂ deficiency in addition; however there was no any significant difference between male and female patients.¹⁴ Similarly, Agrawal L et al ascertained that out of a hundred anemic patients, 55% of patients were diagnosed with vitamin 12 deficiency and 8% with folate deficiency.¹⁹ Deepankar et al found 54%, 25%, and 21% of participants with vitamin B₁₂ deficiency, folic acid deficiency, and combined vitamin B₁₂ and folic acid

deficiency respectively.¹³ A study by Wyckoff KF et al reported subjects with small bodily fluid vitamin B₁₂ is probably going to be while not pathology throughout the amount of post fortification and folic acid fortification led to macrocytosis; correction involving vitamin B₁₂ insufficiency.¹⁸ A review study by Batool S et al reported vitamin B₁₂ and folic acid deficiency is the factor to blame for impaired DNA synthesis, ineffective erythropoiesis, and intramedullary haematolysis that ultimately breaks red blood cells.¹¹

Of the 54 cases on peripheral blood smear, 41 cases had macrocytic anemia and 13 cases had normocytic anemia. These macrocytic and normocytic anemias showed characteristic features such as hyper-segmented neutrophils, polychromatic cells, basophilic stippling and teardrop-shaped cells. Similarly, in megaloblastic anemic patients in one study, macrocytes were common in 88% of patients, and hyper-segmented neutrophils were observed in 43 patients.¹³ A study by Agrawal et al. also showed similar findings.¹⁹

Aslinia F et al. defined macrocytic anemia as a condition of anemia characterized by the presence of abnormally large red blood cells, which is generally detected by an automatic cell counter and peripheral blood smear examination. Careful examination of peripheral blood smear, including red blood cell morphology, cellular components, and the specific properties of the smear, provides important information about the possible etiology of the anemia.²⁰ This study found that the total number of reticulocytes in patients with macrocytic anemia was $4.11 \pm 2.81\%$ with $5.01 \pm 2.85\%$ in men and $4.76 \pm 3.01\%$ in women, and a maximum value in the age group from 18 to 25 years ($4.76 \pm 3.92\%$). While the minimum in the age group over 60. In contrast to our study, Rairikar SS et al. showed about 62.5% of cases of severe anemia with normal reticulocytes,

while 9.4% had low and 28.12% had increased number.²¹

Similarly, D'Onofrio et al. and Balci YI et al. showed that reticulocytes can be a useful marker for differentiating between iron deficiency anemia and vitamin B₁₂ deficiency anemia.²³ In this study, the gender-wise distribution of hemoglobin, RBC indices, peripheral blood smear, and reticulocytes showed no vital variations between male and female patients. In contrast, blood vitamin B₁₂ and folic acid levels were found to be statistically significant ($p < 0.05$) in male and female anemic patients. A study by Sukla et al shows an analogous finding that is comparable our study.²⁴

CONCLUSION

In this study, we determined the maximum incidence of macrocytic anemia in young women. Red blood cell markers such as MCV, MCH, Hemoglobin, reticulocyte fraction, and peripheral blood smear are important diagnostic factors for anemia to help in diagnosis of megaloblastic anemia, so clinical, hematological, and biochemical parameters are important tools for diagnosing macrocytic anemia and further help distinguish megaloblastic anemia from non - megaloblastic anemia.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

LN - Principal Investigator
MWS - Manuscript Writing

ORIGINAL ARTICLE**PROBLEM BASED LEARNING- STUDENT PERSPECTIVE**¹Pushpa Goswami, ¹Fahmida Gul, ¹Farhana Rajpar¹Department of Anatomy, Liaquat University of Medical and Health Sciences, Jamshoro**Corresponding Author:****Dr Pushpa Goswani**, MBBS, M. Phil (Anatomy)

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Article received on: 22-06-2020**Article accepted on:** 15-12-2020

RESULT: Out of 151 medical students, 55.63% strongly disagree that PBL is difficult to acquire knowledge, meanwhile, 36.2% strongly agree the PBL enhances their communication skills and 52.32% students strongly agree that it is better to improve their understanding of topic. In present study, out of 151 students, 18(11.9%) strongly agree and 70(46.4%) just agreed that PBL is time consuming. Among 70 (46.4%) who agreed that PBL is time consuming, 18(11.9%) also agree that it improves understanding of

ABSTRACT**OBJECTIVE:**

To determine the student perspective regarding problem-based learning as teaching methodology in medical teaching.

METHODS:

This prospective study was conducted on medical students at LUMHS Jamshoro from February 2019 to April 2020. This study conducted on 151 volunteer students of first and second year MBBS (n=151). Students enrolled in programs other than MBBS were excluded. Predesigned proforma administered among students to determine their perspective regarding problem-based learning as student centered teaching methodology. Data analysis done on SPSS version 22.0. Frequency % calculated for qualitative variables. Qualitative data compared by applying chi square test. P value <0.05 taken as statistically significant.

topic while 18(11.9%) strongly agree that it improves better understanding of topic. (p value <0.01).

CONCLUSION: The results of this study revealed students' satisfaction with the PBL as better teaching strategy for better learning of students.

KEYWORDS: student perspective, problem based learning, medical students.

Article Citation:

Goswani P, Gul F, Rajpar F, Problem based learning- student perspective. JIMC. 2020 3(2): 13-18

INTRODUCTION

Students' tactics for getting knowledge are vital to the course of learning. Preceding research has displayed that inducing students' methods for deep learning is a multifaceted process and appears considerably more tough than anticipated, even in student-activating learning atmospheres. Evidence based research on academia has revealed that learning methods are wedged not only by learning environment, but also by how the students observe and perceive it. Nevertheless, the way in which it is perceived by students and students' learning approaches is poorly understood.¹ Problem based learning (PBL) is most usually used in medical education to enhance self-regulated learning skills. Self-efficacy ideologies spot students' inspiration with assistance of supervisory courses.² Its mandatory for future physicians and surgeons to have cognitive and intellectual capabilities that comprise problem solving as well as timely decision making skills with comprehensive clinical judgment. They also have a general responsibility and commitment to continue their skills and clinical knowledge by way of appealing in life-long learning.³ PBL benefits students for emerging operative problem solving skills and for appealing active participation in class as well as also empowering them to concept knowledge by their own efforts.⁴ Various graduation curricula comprise PBL as a mainstay in their curricula. Undergraduate students, think PBL as this is a transformation from teacher centered to student centered teaching methodology. Numerous studies undertaken to learn about insights in addition to mid-term test concerts of academy students registered in substantial education classes when PBL is used against old-style teaching approaches.⁵ PBL is one of the teaching methodologies in which the students practice their own efforts to solve the problem/ clinical scenario or case to outline

their own objectives for learning purpose. So, they perform self-directed independent studies before presenting and discussing provided clinical scenario or problem in class. Subsequently, return to their group to debate and present their efforts to solve the provided problem to improve their learned information in lectures and self study.⁶ As PBL is becoming more extensive in use across medical curricula, it is principally very significant to understand the influence that such methods have on students' enthusiasm as well as motivation for learning. This study has been designed to identify the students' perspective regarding benefits of adopting problem based learning in our curricula.

METHODOLOGY

This prospective study was conducted on medical students at LUMHS Jamshoro from February 2019 to April 2020. This study conducted on 151 volunteer students of first and second year MBBS attending PBL classes regularly in Anatomy, Physiology and Biochemistry. Students enrolled in programs other than MBBS and those who do not attend PBLs were excluded. Predesigned proforma administered among students to determine their perspective regarding problem-based learning as student centered teaching methodology. Perspective of students towards PBL was measured with help of 5-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = not sure, 4 = agree, and 5 = strongly agree). Data analysis done on SPSS version 22.0. Frequency % calculated for qualitative variables.

RESULTS

Out of 151 medical students, 55.63% strongly disagree that PBL is difficult to acquire knowledge as shown in **figure 1**. While 36.2% strongly agree the PBL enhances their communication skills as shown in **figure 2**. And

52.32% students strongly agree that it is better to improve their understanding of topic as shown in **figure 3**.

In present study, out of 151 students, 18(11.9%) strongly agree and 70(46.4%) just agreed that

PBL is time consuming. Among 70 (46.4%) who agreed that PBL is time consuming, 18(11.9%) also agree that it improves understanding of topic while 18(11.9%) strongly agree that it improves better understanding of topic. (p value <0.01) **Table No. 1**

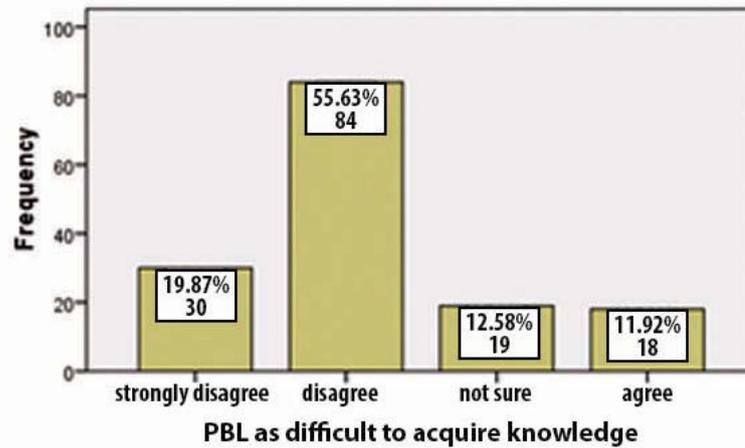


Figure No.1: Frequency % of students' perspective regarding PBL as difficult to acquire knowledge

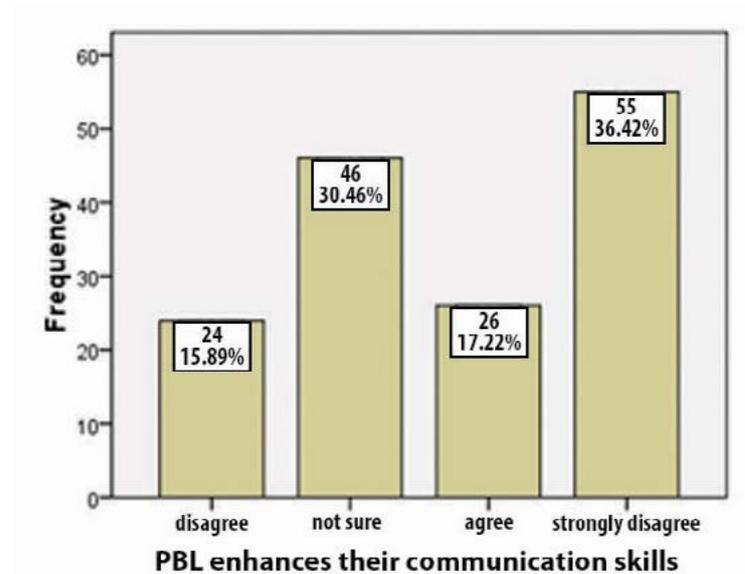


Figure No.2 : Frequency % of students' perspective regarding PBL enhances their communication skills

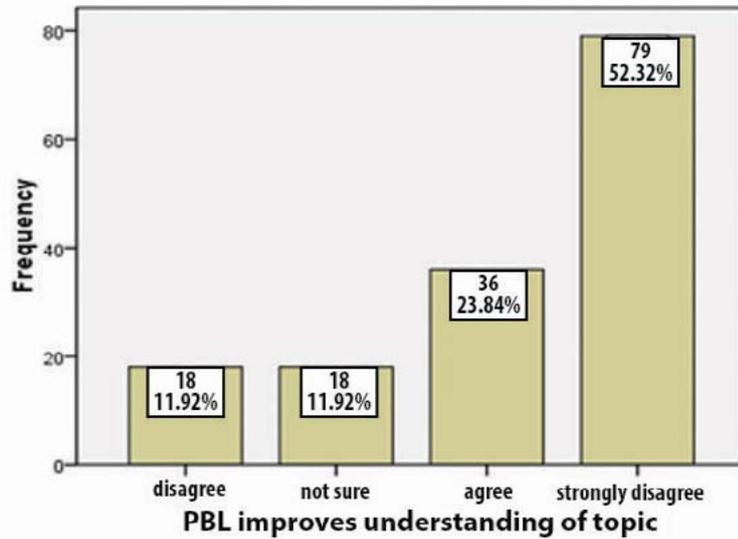


Figure No.3 : Frequency % of students’ perspective regarding PBL that it improves understanding of topic(n=151)

Table No. 1: Comparison of PBL as improving understating of topic with time consuming from student perspective(n=151)

Crosstab

			PBL improves understanding of topic				Total
			disagree	not sure	agree	strongly agree	
PBL is time consuming	strongly disagree	Count	9	0	0	0	9
		% of Total	6.0%	.0%	.0%	.0%	6.0%
	disagree	Count	0	0	0	18	18
		% of Total	.0%	.0%	.0%	11.9%	11.9%
	not sure	Count	0	0	18	18	36
		% of Total	.0%	.0%	11.9%	11.9%	23.8%
	agree	Count	0	18	18	34	70
		% of Total	.0%	11.9%	11.9%	22.5%	46.4%
	strongly agree	Count	9	0	0	9	18
		% of Total	6.0%	.0%	.0%	6.0%	11.9%
Total		Count	18	18	36	79	151
		% of Total	11.9%	11.9%	23.8%	52.3%	100.0%

P value <0.01 Chi square value 1.500 with df=12

DISCUSSION

PBL is one of the pedagogical approaches for facilitating and improving teaching outcomes.⁷ In present study, among 70 (46.4%) students who agreed that PBL is time consuming, 18 (11.9%) also agree that it improves understanding of topic while 18 (11.9%) strongly agree that it improves better understanding of topic. Out of 151 medical students, 55.63% strongly disagree that PBL is difficult to acquire knowledge. Chang BJ.⁸ revealed that PBL is a rational footstep in the direction of emerging students' capabilities to make and integrate their basic concepts in the clinical medicine. Harvard's newly reformed 1 year pre-clinical curriculum has been lifted towards PBL instead of traditional lectures. According to his research, PBL has been playing pivotal positive role regarding learning by way of PBL but he still concluded with need for improvement and constant modification in conducting PBLs by identifying their students' perspectives and needs. Similar study conducted on biomedical students by Sockalingam N and Schmidt HG.⁹ to identify students' needs and their perception as well as insight into what stimulates or supports the students to learn so that they can integrate accordingly to meet their needs for better learning in future problems and also for designing upcoming clinical scenarios or problems for PBLs.

PBLs started almost 30 years back 1970s' as training-oriented learning standards and highlights dynamic learning methods without straightforward starts or endings.¹⁰

The problem-based learning (PBL) approach was implemented as a treatment for advanced teaching graphic arts students in one semester to determine the effects of PBL in improving their creative rational and critical cognition outlook among students. Subsequently they concluded with PBL as playing positive role

in improving creative thought process but instead critical thinking character found not much effective in these students.¹¹ Khoiriyah AJ, Husamah H. concluded regarding PBL that it expands problem solving as well as creative skills among the students, further it was concluded that implementing PBLs even in seven grade students can improve students' learning outcomes.¹²

CONCLUSION

The results of this study revealed students' satisfaction with the PBL as better teaching strategy for better learning of students.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

PG - Principal Investigator

FG - Manuscript Supervision

FR- Manuscript Writing

ORIGINAL ARTICLE**ETHYLENEDIAMINETETRAACETIC ACID (EDTA) – INDUCED PSEUDOTHROMBOCYTOPENIA – A ROUTINE CHALLENGE**

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Assistant Professor, Department of Physiology
Isra University, Hyderabad**Article received on:** 12-06-2020**Article accepted on:** 12-12-2020**ABSTRACT****INTRODUCTION:**

Pseudothrombocytopenia is a condition in which false platelet count occur. EDTA – dependant – pseudothrombocytopenia is because of agglutination of anti-platelet antibodies due to its reaction with platelet in EDTA – anticoagulant blood.

OBJECTIVE:

To see the effect of ethylenediaminetetraacetic acid (EDTA) on platelet clumping in patients with pseudothrombocytopenia.

MATERIALS AND METHODS: This was a prospective study conducted at Department of Pathology, Indus Medical College, Tando Muhamamd Khan over a period of 6 months. Patients with pseudothrombocytopenia on Hematology Analyzer were cross-checked with standard microscopy for confirmation of pseudothrombocytopenia. The samples were also collected in citrate and heparin tubes for evaluation. The data was analyzed using SPSS 24.0.

RESULTS: A total of 90 patients were selected for the study. Patients were aged between 16 to 60 years. Females were more prevalent as compared to males with male to female

ratio of 1:1.8 (Figure 1). Mean age of patients was 41.49 ± 5.3 years. Platelet counts were evaluated from samples collected immediately in all anticoagulants (Table 1) and after 4 hours (Table 2).

CONCLUSION: Patients showed significant effect of EDTA anticoagulant on platelet clumping. Patients with thromcytopenia that do not correlate clinically, must be cross-checked by standard microscopy for confirmation of pseudothrombocytopenia.

KEYWORDS:

Pseudothrombocytopenia, thrombocytopenia, EDTA, anticoagulant, platelets.

Article Citation:

Shaikh A, Talpur AR, Ethylenediaminetetraacetic Acid (EDTA) – Induced Pseudothrombocytopenia – A Routine Challenge. JIMC.2020;3(2): 19-23

INTRODUCTION

Pseudothrombocytopenia is defined as falsely reduced count of platelets with absence of clinical findings such as ecchymoses or petechiae which is caused by inadequate measurements. Platelet clumping and presence of giant platelets are the main causes of falsely decrease in platelet counts. ⁽¹⁾

Platelet clumping is most commonly seen when blood is collected in ethylenediaminetetraacetic acid (EDTA) anticoagulant. This is caused by anticoagulant dependant agglutinins, which include immunoglobulins (IgM, IgA and IgG). ⁽¹⁻²⁾ Clumping of platelets depends on time and also relies upon use of instrumentation for automated counting of platelets. ⁽³⁻⁵⁾ Among all cases of isolated thrombocytopenia in hospitalized patients, pseudothrombocytopenia accounts between 0.01 - 2% cases. ⁽¹⁾ In absence of clinical features, evaluation of decreased platelets number is necessary. Visual examination by peripheral blood smear will be accurate to rule out the presence of pseudothrombocytopenia so that unnecessary treatment can be avoided. ⁽²⁾ In such circumstances, use of alternative anticoagulation may help in more accurate estimation of platelet estimation. ^(2,6) Therefore, this study is designed to evaluate the effect of EDTA on platelet clumping, resulting in pseudothrombocytopenia.

MATERIALS AND METHODS

This was a prospective study conducted at

Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan. The study was conducted for period of 6 months (February 2020 to July 2020). Blood samples were collected in EDTA tubes and evaluated by automated haematology analyzer. Patients with low platelet counts without any clinical features of thrombocytopenia were included. Peripheral blood smears were performed for all cases of thrombocytopenia. Wright's stain was used for preparation of slides and examined by 2 pathologists.

Patients with false low count of platelets due to clumping were filtered. Additional blood samples were collected in heparin tubes and sodium citrate tubes. Correction for sodium citrate dilution was performed by multiplication of obtained number with multiplication factor 1.1 ($n \times 1.1$). These samples were also automated haematology analyzer. After 4 hours of collection, the samples were again analyzed for the evaluation of time dependant influence. The data was analyzed using SPSS 24.0.

RESULTS

A total of 90 patients were selected for the study. Patients were aged between 16 to 60 years. Females were more prevalent as compared to males with male to female ratio of 1:1.8 (Figure 1). Mean age of patients was 41.49 ± 5.3 years. Platelet counts were evaluated from samples collected immediately in all anticoagulants (Table 1) and after 4 hours (Table 2).

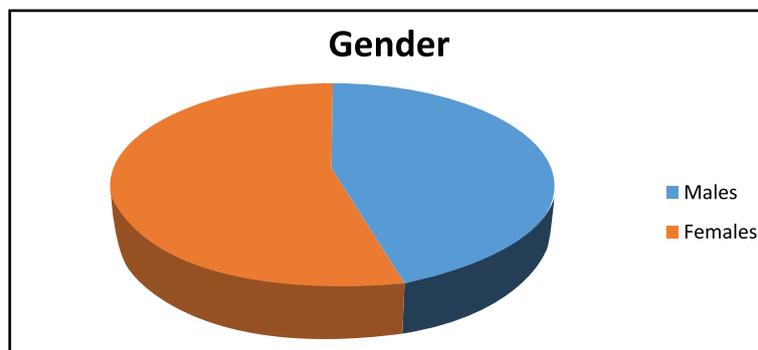


Figure 1: Gender Distribution (n=90)

Table 1: Values of Platelets in Various Anticoagulants Immediately After Collection (n=90)

Anticoagulants	Minimum	Maximum	Mean
EDTA	25,000	1,38,000	1,01,000
Citrate	47,000	3,51,000	1,57,000
Heparin	33,000	2,27,000	1,23,000

Table 2: Values of Platelets in Various Anticoagulants after 4 Hours of Collection (n=90)

Anticoagulant	Minimum	Maximum	Mean
EDTA	49,00	1,18,000	58,000
Citrate	44,000	2,43,000	1,38,000
Heparin	31,000	2,03,000	1,08,000

DISCUSSION

Pseudothrombocytopenia can be caused by various reasons such as inadequate sampling of blood, clumping or satellitism of platelets or due to giant platelets. Clumping of platelets may also be due to EDTA – anticoagulant or cold agglutinin. Anti-platelet antibodies are the main cause of pseudothrombocytopenia due to EDTA. ^(1, 3-4)

The activator for production of antibodies is not known and can rise in response to different antigen, followed by cross-reactivity with platelets causing agglutination. ⁽²⁾ The complete and exact mechanism of antibody reaction with antigens on membranes of platelets is not understood. It is postulated that when EDTA is mixed with platelets, persuade a conformational variation in membrane that results in “neoantigens” exposure to which antibody binds. ^(2, 5) In patients with Glanzmann thrombasthenia, there is no reaction of platelets with these antibodies which suggests that glycoproteins on platelet membrane, GpIIb or GpIIIa, which are not present in these patients, may be “neoantigens” in pseudothrombocytopenia. ⁽⁶⁾ It is postulated that the binding site for antibody to GpIIb is usually not visible in GpIIa-GpIIIa complex and

so the complex must separate before binding of antibody occur. ⁽⁷⁾ The EDTA concentration, drugs, temperature and pH may fluctuate the dissociation of complex. ⁽⁸⁾ it is also been alleged that clumping of platelets induced by EDTA can be separated by mixing calcium chloride in order to re-associate the complex of GpIIb-GpIIIa and sodium heparin to maintain the anticoagulant effect for exact platelet count estimation. ^(9, 14) Likewise, the count of platelets in pseudothrombocytopenia has been performed by adding aminoglycosides. ^(1, 9-10)

In current study, the pseudothrombocytopenia caused by EDTA was more prevalent in females than in males. Similarly, Berkman et al showed more female predominance in his study. ⁽²⁾ In our study, the samples anticoagulated with EDTA revealed decreased count of platelets and mean count of platelets as compared to heparin and citrate anticoagulated samples. Citrate is considered to have better anticoagulant activity for reduction of pseudothrombocytopenia in various studies. ^(1, 9, 11) In few studies, the count of platelets was increased in magnesium sulphate anticoagulated samples as compared to EDTA. ⁽⁹⁾ The routine estimation of mean platelet volume (MPV) is performed in by majority of automated haematology

analyzers and is very useful to differentiate idiopathic thrombocytopenic purpura (ITP) or other etiologies of thrombocytopenia from pseudothrombocytopenia. ^(2, 12) Few studies also support the time dependant effect of EDTA anticoagulation which also leads to change in mean platelet volume (MPV). ^(1, 9)

In our study, decrease in platelet counts was seen in EDTA samples as compared to samples anticoagulated with heparin and citrate after 4 hours of collection. These findings are also supported by other studies. ^(1, 2, 9, 13) Clumping of platelets seen on peripheral film is helpful in diagnosis of pseudothrombocytopenia caused by EDTA. ^(9-10, 14-15) The term "EDTA – dependant thrombocytopenia" was used by Berkman for the condition of in vitro aggregation of platelets with the use of blood anticoagulated with EDTA. ⁽²⁾ Various other terms were also used by other researchers, including "anticoagulant – induced pseudothrombocytopenia" by Schrezenmeir and "laboratory diseases" by Gschwandtner et al. ⁽¹⁶⁻¹⁷⁾

CONCLUSION

EDTA-anticoagulation showed significant platelet clumping which cause pseudothrombocytopenia. Peripheral blood smears are usually not evaluated by standard microscopy and they remain ignored if histograms or warning flags of automated haematology analyzers are not evaluated adequately. Due to this ignorance, pseudothrombocytopenia caused by EDTA is undiagnosed which ultimately leads to unwanted investigations, unnecessary blood transfusions and hold back of emergency surgical procedures. In these circumstances, patients may suffer discomfort and extra cost. Peripheral blood smears should be evaluated properly for the evaluation of clumping and/or aggregation of platelets in patients with no clinical picture of thrombocytopenia.

Conflict of Interest: None

Funding Source: None

Acknowledgment: I would like to thank my colleagues and technical staff for their help.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

AS - Principal Investigator

RAT - Manuscript Writing

ORIGINAL ARTICLE**MIGRAINE AND VITAMIN D STATUS**Keenjher Rani¹, Urooj Bhatti¹¹Department of physiology, Liaquat University of Medical and Health Sciences, Hyderabad**Corresponding Author:****Dr. Keenjher Rani,**

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Article received on: 19-06-2020**Article accepted on:** 09-11-2020**ABSTRACT****BACKGROUND:**

Migraine had been well-known as the primary foremost debility cause for headache globally.

OBJECTIVE:

To determine the vitamin D status among the migraine patients with aura and without aura.

METHODOLOGY:

This cross-sectional comparative study has been conducted at LUMHS Jamshoro, from 6/6/2018 to 7/01/ 2020. This study comprised all male and female migraine patients of age group 18-45 years. Migraine was diagnosed conferring to strategies of international headache society. Exclusion criteria for this study were headache

other than migraine, neurologic deficit or psychiatric comorbidities, hypertensives, and diabetics. Informed consent taken from all the study participants prior to clinical consultation. Migraine patients inquired for severity of migraine on the basis of presence of aura and without aura, followed by clinical neurological examination. After taking all aseptic measures, 03 ml of blood taken intravenously in study population and referred to Diagnostic and Research Laboratory of LUMHS Jamshoro. Serum vitamin D3 levels determined by using 3L52 ARCHITECT 25 -OH Vitamin - D Reagent

kit. Vitamin D3 levels more than 75 ng/ml considered sufficient, while, 35 to 75 ng/ml as sub optimal and in the range of 20&30ng/ml as Vitamin D insufficiency and levels < 20 ng/ml considered deficient. The data entered in predesigned proforma and analyzed on SPSS 22.0. Vitamin D status compared among the migraine patients with aura and without aura by applying chi square test. Vitamin D3 levels compared between migraine patients with aura and without aura by applying independent t-test

Article Citation:

Rani K, Bhatti U. migraine and vitamin d status. JIMC. 2020; 3(2): 24-29

RESULT:

Mean age of migraine patients (n=84) was 32.3 ± 3.5 years and out of them, 36 (42.9%) were males and 48 (57.1%) were females. Frequency % of vitamin D sufficiency was 7 (8.3%), sub-optimal was 22 (26.2%), vitamin D insufficiency was 29 (34.5%) and vitamin D deficiency was 29 (31.0%). Out of 84 migraine patients, 69 were with aura and 15 were without aura. Out of 69 migraine patients with aura, 25 (29.8%) were vitamin D deficient, 28 (33.3%) were vitamin D insufficient, 13 (15.5%) found with sub optimal levels and only 3 (3.6%) with vitamin D sufficiency while among those without aura (n=15), 1 (1.2%) were vitamin D deficient, 1 (1.2%) were vitamin D insufficient, 9 (10.7%) with sub optimal vitamin D levels and 4 (4.8%) with sufficient vitamin D. (p value <0.01).

CONCLUSION:

Vitamin D has been revealed more deficient and insufficient in migraine patients with aura as compared to those migraineurs without aura.

KEYWORDS: Migraine, Vitamin D deficient, vitamin D sufficient

INTRODUCTION

Migraine had been well-known as the primary foremost debility cause for headache globally. A diversity of nutritional complements also been familiarized for the purpose of relieving from migraine; one of them is vitamin D which has anti-inflammatory as well as antioxidant properties and focus of research in current time.^{1, 2} Role of vitamin D in homeostasis of calcium as well as in bone metabolism had been proven fact while its part in migraine is center of controversy.³ Migraine is neurovascular ailment that distresses 6% of the males and 18% of female gender globally. Lack of numerous dietary agents in diet, i.e., magnesium, niacin,

cobalamin, co enzymes Q10, carnitine, alpha lipoic acid and vitamin D found to be associated with development of migraine. Some researchers postulate that mitochondrial dysfunction and impaired antioxidant status can cause migraine.⁴ Migraine with aura, has been connected to amplified hazard for developing ischemic cerebrovascular disease.⁵ In one of the randomized controlled trial study, Vitamin D3 revealed as significantly reducing the duration of migraine attack. Still, further research is required to explore and confirm about the prophylactic role of vitamin D in migraine.⁶ This study has been designed to determine the vitamin D levels among the migraine patients with aura and without aura.

METHODOLOGY

This cross-sectional comparative study has been conducted at LUMHS Jamshoro, from 6/6/2018 to 7/01/2020. The sampling technique was convenient purposive sampling. This study comprised all male and female migraine patients of age group 18-45 years. Migraine was diagnosed conferring to strategies of international headache society. Exclusion criteria for this study were headache other than migraine, neurologic deficit or psychiatric comorbidities, hypertensives, and diabetics. Informed consent taken from all the study participants prior to clinical consultation. Migraine patients inquired for severity of migraine on the basis of presence of aura and without aura, followed by clinical neurological examination. After taking all aseptic measures, 03 ml of blood taken intravenously in study population and referred to Diagnostic and Research Laboratory of LUMHS Jamshoro. Serum vitamin D3 levels determined by using 3L52 ARCHITECT 25 -OH Vitamin - D Reagent kit. Vitamin D3 levels more than 75 ng/ml considered sufficient, while, 35 to 75 ng/ml as sub optimal and in the range of 20 & 30 ng/ml

as Vitamin D insufficiency and levels < 20 ng/ml considered deficient. The data entered in predesigned proforma and analyzed on SPSS 22.0. Vitamin D status compared among the migraine patients with aura and without aura by applying chi square test. Vitamin D3 levels compared between migraine patients with aura and without aura by applying independent t-test.

RESULT

Mean age of migraine patients(n=84) was 32.3±3.5 years and they were 36(42.9%) were males and 48(57.1%) were females. Frequency % of vitamin D sufficiency was 7 (8.3%), sub-optimal was 22(26.2%), vitamin D insufficiency was 29(34.5%) and vitamin D deficiency was 26(31.0%). Mean and sd of vitamin D levels was 30.15±21.5nmol/lit. Out of 84 migraine patients,

69 were with aura and 15 were without aura.

Table No. 1

Vitamin D3 levels compared according to severity of migraine i.e., with aura and without aura and p value was 0.05 that is close to significant. **Table No. 2**

Out of 69 migraine patients with aura, 25(29.8%) were vitamin D deficient, 28(33.3%) were vitamin D insufficient, 13(15.5%) found with sub optimal levels and only 3(3.6%) with vitamin D sufficiency while among those without aura(n=15), 1(1.2%) were vitamin D deficient, 1(1.2%) were vitamin D insufficient, 9(10.7%) with sub optimal vitamin D levels and 4(4.8%) with sufficient vitamin D.(p value <0.01)

Table No.3

TABLE NO.1: DESCRIPTIVE STATISTICS OF MIGRANEURS (N= 84)

	Mean ±Sd	Frequency (%)
Age (in Years)	32.3±3.5	--
Gender		
Male	--	36 (42.9%)
Female	--	48 (57.1%)
Vitamin D sufficiency	--	7(8.3%)
Sub optimal	--	22(26.2%)
Vitamin D insufficiency	--	29(34.5%)
Vitamin D deficiency	--	26(31.0%)
Vitamin D levels(ng/ml)	30.15±21.5	--
Migraine with aura	--	69(82.1)
Migraine without aura	--	15(17.9)

TABLE NO. 2: VITAMIN D3 LEVELS IN MIGRANEURS WITH AURA AND WITHOUT AURA

	Migraine severity	N	Mean	Std. Deviation	P value ^a
Vitamin D3	with aura	69	28.07	20.1	0.05
	without aura	15	39.70	25.9	

TABLE NO.3 : COMPARISON OF VITAMIN D STATUS IN MIGRAINE PATIENTS WITH AURA(N=69) AND WITHOUT AURA (N=15)**Vitamin D staus * migraine Crosstabulation**

			Migraine		Total
			with aura	without aura	
Vitamin D Status	Vitamin D sufficiency	Count	3	4	7
		% of Total	3.6%	4.8%	8.3%
	Sub optimal	Count	13	9	22
		% of Total	15.5%	10.7%	26.2%
	Vitamin D insufficiency	Count	28	1	29
		% of Total	33.3%	1.2%	34.5%
	Vitamin D Deficiency	Count	25	1	26
		% of Total	29.8%	1.2%	31.0%
Total	Count		69	15	84
	% of Total		82.1%	17.9%	100.0%

P- value <0.01 with df=3 and pearson chisquare value=22.91

DISCUSSION

Migraine is one of the most common disabling neurological disorders. It is characterized by recurrent episodes of headache, variable in duration, intensity, and frequency, and is accompanied by nausea, vomiting, photophobia, and/or phonophobia. In some cases, migraine attacks are preceded by focal neurological symptoms called aura.⁷ In present study, among migraine patients with aura, 29.8% has been found with deficient vitamin D levels and 33.3% with vitamin D insufficiency.

Özer G. 8revealed that average vitamin D level was 7.4 ng/ml among patients with migraine with aura group and 8.5 ng/ml in patients with migraine without aura. Severe vitamin D deficiency was detected in 14 (66.7%) with aura. Similar to this study, Elsayed et al.⁷ also found deficient vitamin D levels in patients of migraine with aura. A variety of dietary supplements have been introduced for

migraine complementary treatment. As an anti-inflammatory and antioxidant agent, vitamin D is one of these agents which has been of interest in recent years. Even though, increased proportion of vitamin D deficiency and vitamin D insufficiency has been emphasized previously in past literature among the patients of migraine as related to controls, still, no consensus has been observed in recommending vitamin D practically in clinical practice.⁶ Migraine patients have a tendency to evade sunlight ultraviolet rays because of photophobia during migraine episode. Decreased physical activity and extended at work hours deceptively increase the risk for developing headache or migraine.^{9,10} Vitamin D is recommended to show significant part in release of dopamine and serotonin. Both dopamine as well as serotonin has been proposed as neurotransmitters which are involved in the pathogenesis of migraine. The occurrence of vitamin D receptors (VDR) in

hypothalamus (concerned with pain sensation), support the supposition of vitamin D influence in patients of migraine. VDR is nuclear protein and the associated gene is situated on chromosome 12q & this bears numerous polymorphisms.¹¹VDR with vitamin D binding protein in hypothalamus and existence of alpha 1-hydroxylase enzyme as well as and decreased magnesium levels are the mechanism about the connotation between Vitamin D deficiency and migraine. Because intestinal absorption of magnesium is dependent on Vitamin D.¹² Well-known role of calcium in contraction of smooth muscle cells in the walls of blood vessels causing vasoconstriction might provide a coherent connection of vitamin D deficiency with migraine attacks.⁵ Migraine headaches are one of the most common reason for disability globally, culminating in compromised quality of life with grave commercial consequences.¹³ Further research is the prerequisite of time to reveal about vitamin D status and role of other micronutrients in migraine patients to recover the quality of life among migraineurs in coming future.

CONCLUSION

Vitamin D has been revealed more deficient and insufficient in migraine patients with aura as compared to those migraineurs without aura.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

KR - Manuscript Writing

UB - Principal Investigator

ORIGINAL ARTICLE**ETIOLOGIES OF POST MENOPAUSAL BLEEDING IN TERTIARY HOSPITAL**¹Nida Zaki, ¹Uzma Brohi, ²Zahida Brohi¹Department of Gynae and Obstetrics, Isra University Hospital, Hyderabad²Department of Gynae and Obstetrics, Bilawal Medical College, Hyderabad**Corresponding Author:****Dr Nida Zaki,**

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Article received on: 04-05-2020**Article accepted on:** 14-12-2020**ABSTRACT****OBJECTIVE:**

Evaluation of the frequency of common etiologies of post menopausal bleeding in women coming to Isra University Hospital Hyderabad.

BACKGROUND:

To ensure the absence of serious complication like malignancy and endometrial hyperplasia, Postmenopausal bleeding requires complete assessment and evaluation.

RESULTS:

The most proportion of patient were found in age of between 50 – 60 years. About 5.3 % of patients were grand multiparas .the most common etiology in our study s endometrial hyperplasia 46.2 %.

CONCLUSION:

Our current study demonstrate that the high prevalence of endometrial hyperplasia, these patients needs careful evaluation in order to avoid serious complication like endometrial carcinoma.

KEYWORDS: Post Menopausal Bleeding, Endometrial Hyperplasia

INTRODUCTION:

Postmenopausal bleeding is defined as bleeding that's occurs after twelve months of amenorrhea in a women of age in whom menopause is expected. ⁽¹⁾

According to a retrospective study carried

out in Singapore published in Singapore MEDJ 1995, abnormal bleeding is one of the most common presenting complaints encountered in a gynecological clinic. ⁽²⁻³⁾ Amongst them, post menopausal bleeding ranks the most sinister as it often associated

Article Citation:

Zaki N,Brohi U,Brohi Z, etiologies of post menopausal bleeding in tertiary hospital.JIMC. 2020;3(2): 30-35

with malignancy. ⁽⁴⁾ Post menopausal bleeding is not a normal physiological phenomenon. Any bleeding should be considered abnormal in postmenopausal women except for those with predictable withdrawal bleeding taking hormone replacement therapy. ⁽⁵⁾

According to a study carried out in Lahore, Pakistan published in ANNALS, about 10% of women with postmenopausal bleeding have a primary or secondary malignancy. The study of 50 cases with postmenopausal bleeding at Lady Willingdon2 Hospital Lahore Pakistan showed that 36 % of patients were found to have malignancy, out of which endometrial carcinoma was 28 % and carcinoma cervix was 8 %. This study showed a very high prevalence of malignancy. Study showed that among benign causes endometrial hyperplasia was the commonest one and was found in 26% of cases, endometrial polyp was found in 8 % . Another study carried out at Fauji Foundation Hospital Rawalpindi the overall incidence of genital tract malignancies was 16 % this is much less than found in the study mentioned above . Non malignant causes were found in 84 % of cases and atrophic vaginitis was the most common finding followed by endometrial polyp 5.1 %, cervical polyp 2.6 % decubitus ulcer at uterovaginal prolapse 1.9 % . At People Medical College and Hospital Nawabshah a study was conducted on 50 cases of postmenopausal bleeding to see the prevalence of malignancy in women with postmenopausal bleeding. They found malignancy in 30 % of cases and benign causes were seen in 48 % of patients. In their study the most common benign cause of post menopausal bleeding was endometrial polyp (12%). ⁽⁶⁻⁹⁾ With review of these studies this becomes clear that there is discrepancy in data of different studies carried out in different parts of the country and these studies are not recent, as we know the postmenopausal bleeding has been changed in western world in recent years, so there is no recent data over this important

issue for our population.

This study is designed to know the current prevalence of common etiologies of postmenopausal bleeding among women of age 50 – 70 years attending the outpatient department of Isra University Hospital Hyderabad

METHODS AND MATERIAL

OBJECTIVE: To evaluate the frequency of common etiologies of post menopausal bleeding in women coming to Isra University Hospital Hyderabad.

SETTINGS: The study will be conducted in the department of Obstetrics and Gynecology at Isra University Hospital Hyderabad from January 2019 to July 2019. The sample technique was Non Probability consecutive sampling. All women presenting with spontaneously post menopausal bleeding after one year of menopause with intact uterus and ovaries of age ranging from 50 to 70 years and irrespective of parity will be included in study. Women were excluded those having genital tract trauma, Women having coagulation disorder Women with radiotherapy or chemotherapy induced menopause, Women with medical co-morbidities like liver disorder or congestive heart failure, Women on medication such as digitalis and spironolactone and Women with diagnosed genital tract carcinoma. The study has been approved by the ethical review committee of Isra University Hospital and a certificate of approval has been issued by the institute . Women who fulfill the inclusion criteria will be included from the outpatient department of Isra University Hospital after taking the informed consent from them. Details of patients regarding age, parity, interval between last menstrual period and onset of including the speculum and bimanual vaginal examination. Trans abdominal ultrasound will be arranged for measurement of endometrial thickness, presence of focal mass, cystic spaces and fluid in the endometrial cavity will be noted. All the information will be entered in

predesigned proforma and analyzed by using SPSS version 15.0. mean + SD will be calculated for age and duration of menopause. frequency will be calculated for common etiologies of PMB and for parity. Effect modifiers like age, duration of menopause will be dealt by through stratification. Chi square test will be applied post stratification. P value equal to less than 0.05 will be taken as significant. result will be checked at 95 % confidence interval.

RESULTS:

Out of 197 patients most of PMB bleeding patients were between ages of 50 to 60 years. Maximum number of patients were in 5th decade and mostly were grand multiparus (50.3%). The most common etiology of PMB in our study is endometrial hyperplasia (46.2%)

and mean interval of LMP and PMB were 6.5 years. In our study time lapse between onset of bleeding and hospitalization was 5.0 ± 0.7 weeks. For post stratification test we divided patient in two age group < 60 and more than 60 in relation to causes of postmenopausal bleeding that show significant outcome with p-value of 0.00.(table 4).

Table 1: shows the statistical analysis (frequency) of the age of study participants.

Table 2: shows the frequency of causes of post menopausal bleeding in patients those who attended Isra university Hospital clinics.

Table 3: shows the parity of patients.

Table 1: AGE GROUP (n= 197)

Age Group	Frequency	Percentage
F50 – 60	123	62.4%
61 – 70	56	28.4%
71 – 80	18	9.1 %

TABLE 2: CAUSES OF POST MENUPAUSAL BLEEDING

Causes	Frequency	Percentage
Cervical polyp	28	14.2 %
Endometrial polyp	36	18.3 %
Endometrial hyperplasia	91	46.2%
Endometriosis	42	21.3 %

TABLE 3 : PARITY OF PATIENTS

Parity	Frequency	Percentage
NULLIPARUS	24	12.2 %
PRIMIPARA	3	1.5%
MULTI PARA	71	36.0%
GRAND MULTIPARA	99	50.3 %

**TTABLE: 4 POST STRATIFICATION TEST (CHI SQUARE)
P VALUE = 0.000**

N= 197 < 60YRS (94) >60YRS(103)	CERVICAL POLY	ENDOMETRIAL POLYP	ENDOMETRIAL HYPERPLASIA	ENDOMETRIOSIS
< 60 YEARS	20	22	30	22
>60 YEARS	8	14	61	42

DISCUSSION

Postmenopausal bleeding is a sinister complaint of postmenopausal women. At our current study the mean age of presentation was 58.6 ± 9.3 years which is similar to other many studies. ^(2, 6-8)

A wide range of benign causes were observed related to cervix, vagina and uterus that are consistent with other studies. However Amongst the benign causes Endometrial Hyperplasia is the most common etiology in our study followed by endometriosis as in many other studies. Other study shows that women 18–90 years the overall incidence of endometrial hyperplasia was 133 per 100,000 woman-years, was most common in women ages 50–54, and was rarely observed in women under 30. Simple and complex hyperplasia incidences peaked in women ages 50–54. The incidence of atypical hyperplasia was greatest in 60–64 year old women, and was similar to the peak age-specific incidence of endometrial carcinoma. 4 Decreases in the incidence of endometrial hyperplasia over time were observed, particularly for atypical endometrial hyperplasia, however, in few studies the commest cause were chronic cervicitis. ⁽⁸⁻¹¹⁾

Chronic cervicitis has also been seen as the predominant cause in few studies. The differences might be based on unlike patterns of diseases according to geographic

or ethnic differences or easily as of separate choice criteria in the midst of a choice of examine populations. In orderliness to simplify these differences larger, multicentre studies would be required. Atrophic endometritis requirements no treatment; on the other administer atrophic vaginitis requirements to be treated with neighborhood oestrogen creams, pessaries, medication and oestradiol vaginal rings. Fibroids of innumerable sizes were seen in four patients. They more often than not telescope after menopause but if they enlarge or are linked with blood loss be supposed to be disinterested payable to possible cruel change. ⁽¹²⁾ Endometrial polyp must be aloof to check spiteful change. clear-cut hyperplasia know how to be treated with medicines but nonconforming hyperplasia requires surgical management. Cervical causes built-in decubitus boil owed to uterine prolapse, cervical polyp, carcinoma in situ and carcinoma cervix. Cervical polyp are frequently tiny in extent which bottle be avulsed. ⁽¹³⁻¹⁴⁾

In our setup none of patient were diagnosed as endometrial carcinoma although seen in many other studies. At People Medical College and Hospital Nawabshah a study was conducted on 50 cases of postmenopausal bleeding to see the prevalence of malignancy in women with postmenopausal bleeding. They found malignancy in 30 % of cases and benign causes were seen in 48 % of patients. In their

study the most common benign cause of postmenopausal bleeding was endometrial polyp (12 %).

In our study time descend between onset of blood loss and hospitalization was 5.0 ± 0.7 weeks which is appreciably drop than the reported time slip of 19.2 weeks. It may be right and proper to the detail that the complete our patients are insincere allowed for free remedial treatment, for that reason they are quickly referred by leading thought doctors to our division for investigations and management by the consultant gynecologist. The shorter time interval is a important sentence as it would declare been of fundraiser to extra patients presenting with PMB in phase I & II of endometrial carcinoma. at hand is no sanction for showing all-purpose people for endometrial carcinoma. PMB is mainly regular presenting symptom and a alarm signal for endometrial carcinoma, as a result it helps women to get an experimental health advice.

CONCLUSION

Our current study demonstrate that the high prevalence of endometrial hyperplasia, these patients needs careful evaluation in order to avoid serious complication like endometrial carcinoma.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

NZ - Principal Investigator

UB - Co Author

ZB - Manuscript Writing

ORIGINAL ARTICLE**OUTCOME OF ACUTE PANCREATITIS IN RELATION TO FREQUENCY, ETIOLOGY AND COMPLICATIONS**¹Atta Abbasi, ²Muhammad Ilyas, ³Javaid Iqbal¹*Department of Medicine, Pennine Acute Hospital, Greater Manchester, United Kingdom*²*Department of Pathology, Queens Medical Centre, University of Nottingham.*³*Department of Gastroenterology, Wythenshawe Hospital, Greater Manchester, United Kingdom***Corresponding Author:****Dr Atta Abbasi**, MBBS, FRCP, PhD

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Article received on: 03-04-2020**Article accepted on:** 09-12-2020**ABSTRACT****BACKGROUND:** Acute pancreatitis is one of the main causes of acute abdomen. It may cause multi-organ failure or even death. High morbidity and mortality are associated with it. The research study aimed at evaluating the clinical characteristics and results of acute pancreatitis in our community.**RESULTS:** A total 91 patients were included in this current study. The mean age of patients were 45.34 ± 15.657 years (range: 13–75 years) and majority were males 49 (53.8 %).patient were obese in about 9 % (9.9%).according to etiologist, 44 (48.4%) were have gall stones pancreatitis, 33 (36.3 % were diagnosed as idiopathic pancreatitis and only (9.9 %) found alcohol induce pancreatitis. Pancreatic collection was the common complication in 12(13.2%) patients while 84(92.3%) with interstitial pancreatitis and 7(7.7%) developed necrotic pancreatitis. For billiary pancreatitis 25(27.5%) patients under went ERCP during admission. Overall 84(92.3%) patients improved from pancreatitis (Table 1).**Conclusion:** Acute pancreatitis could have serious outcomes if not correctly and early managed. It is recommended to perform multicenter studies with a large sample of patients. multi-disciplinary team is required to

assess idiopathic pancreatitis.

Keywords: Acute pancreatitis, Gallstones, alcohol induce pancreatitis.**Article Citation:**

Abbasi A, Ilyas M Iqbal J Outcome of Acute Pancreatitis In Relation to Frequency, Etiology and complications. JIMC. 2020;3(2): 36-40

INTRODUCTION

The reported incidence of acute pancreatitis ranges from 4.9 to 35 per 100,000 population in USA¹ the increased rate of acute pancreatitis incidence probably due to increasing of obesity and gallstones worldwide along with increasing ratio with age and male population² although there are many theories regarding the pathogenesis of acute pancreatitis but they all are still controversial, these causes still not yet been completely elucidated³.

Risk factor prevalence is influenced by Geographic and demographic differences between and within countries and it partly defining the variable incidence and etiology⁴. Alcohol induce damage to pancreas is the most leading cause of acute pancreatitis worldwide⁵.

For the diagnosis of acute pancreatitis revised Atlanta classification requires atleast 2 or more of the following criteria be met (a) severe abdominal pain that met the inclusion criteria of acute pancreatitis, (b) .serum lipase and or amylase level greater then twice upper limit of normal, (c) characteristic pattern of imaging of acute pancreatitis⁶. The most common imaging used for acute pancreatitis is CT imaging however magnetic resonance imaging is also appropriate⁷, but if the clinical criteria us met along with biochemical markers then imaging is not nessorcery to make diagnosis of acute pancreatitis⁷.

Acute pancreatitis is categorized into mild, moderate and severe according to their severity scale⁸ by the presence or absence of organ failure with higher mortality rate in case of severe pancreatitis which is account for about 25%⁹.

The aim of this current study is to assess the outcome that are associated with the risk factor in tertiary hospital of Hyderabad.

PATIENTS AND METHODS

All consecutive patients with acute pancreatitis aged above 10 year, of either gender, presenting in the emergency department of isra university hospital were included. Patient diagnosed as carcinoma of pancreas or other malignancy was excluded. Acute pancreatitis is defined as abdominal pain that is typically characteristic of epigastric pain that radiating to the back) with serum lipase levels and amylase level more than three times higher than normal. If the clinical criteria us met along with biochemical markers then imaging is not nessorcery to make diagnosis of acute pancreatitis. After taking informed consent, blood sample for complete blood count, liver function tests, serum albumin, serum amylase and lipase, serum calcium, LDH, lipid profile, random blood sugar, serum creatinine and urea was collected. Ultrasound abdomen was performed to see billiary system.

RESULTS

A total 91 patients were included in this current study. The mean age of patients were 45.34 ±15.657 years (range: 13–75 years) and majority were males 49 (53.8 %). Patient were obese in about 9 % (9.9%). According to etiologist, 44 (48.4%) were have gall stones pancreatitis, 33 (36.3 % were diagnosed as idiopathic pancreatitis and only (9.9 %) found alcohol induce pancreatitis .Pancreatic collection was the common complication in 12(13.2%) patients while 84(92.3%) with interstitial pancreatitis and 7(7.7%) developed necrotic pancreatitis. For billiary pancreatitis 25(27.5%) patients under went ERCP during admission. Overall 84(92.3%) patients improved from pancreatitis (Table 1) .

Table 1. Association of risk factors and local complication w.r.t outcome.

		Outcome		P-value
		Improved	Expired	
Sex	Male	39 (46.4%)	3 (42.9%)	0.86
	Female	45 (53.6%)	4 (57.1%)	
DM	Yes	17 (20.2%)	2 (28.6%)	0.60
	No	67 (79.8%)	5 (71.4%)	
Alcohol	Yes	7 (8.3%)	1 (14.3%)	0.59
	No	77 (91.7%)	6 (85.7%)	
Smoker (Past/Present)	Never Smoke	7 (8.3%)	1 (14.3%)	0.59
	Past Smoker	77 (91.7%)	6 (85.7%)	
U/S GB Stone	Yes	27 (32.1%)	2 (28.6%)	0.85
	No	57 (67.9%)	5 (71.4%)	
CBD Dilatation	Yes	25 (29.8%)	1 (14.3%)	0.38
	No	59 (70.2%)	6 (85.7%)	
Stone In CBD	Yes	20 (23.8%)	1 (14.3%)	0.57
	No	64 (76.2%)	6 (85.7%)	
Peripancreatic Collection	Present	4 (4.8%)	2 (28.6%)	0.02*
	Absent	80 (95.2%)	5 (71.4%)	
Type of Pancreas	Interstitial	80 (95.2%)	5 (71.4%)	0.02*
	Necrotic	4 (4.8%)	2 (28.6%)	
Ascites	Yes	25 (29.8%)	4 (57.1%)	0.14
	No	59 (70.2%)	3 (42.9%)	

P-value < 0.05 will be considered as significant.

DISCUSSION

In this current study we assessed the in hospital mortality related to frequency, etiology and local complications of acute pancreatitis. In our study we found that majority of patients were male with normal BMI and have gall stone pancreatitis along with interstitial pancreatitis.

Gallstones pancreatitis is the most prevalent cause of acute pancreatitis in our current study, which is also similar in many others studies that is account for about 80% of the population¹⁰⁻¹¹⁻¹². acute pancreatitis have a clear gender

bias associations in may previous studies with male predominance in case of alcohol induce pancreatitis and gallstones pancreatitis in females predominance¹³, similar result were observed in our current study (9.9 %) found alcohol induce pancreatitis in males and 44 (48.4%) were have gall stones pancreatitis and majority are females.¹⁴

Peripancreatic Pancreatic collection was the common complication in 12(13.2%) patients while 84(92.3%) with interstitial pancreatitis and 7(7.7%) developed necrotic pancreatitis. Out of 91 patients 7(7.7%) expired . When risk

factors and local complication were associated with outcome, the p value < 0.02 was significant only for local complication while there was no significant association with risk factors.¹⁵

The higher rates of development of local complications among the alcohol AP group has previously been pointed out by various studies. Gullo L et al.¹⁶ found higher rates of peripancreatic fluid collection, Cho et al. highlighted greater pseudocyst formation in the alcohol group. Furthermore, Gullo L et al.¹⁶ compared the CT images of cases of AP between the two groups and found more aggressive CT findings in the alcohol group. Alcoholic AP is usually seen in heavy drinkers in whom substantial pancreatic damage has already set in by the time the patient develops AP.¹⁷

Whether etiology does play a role in the outcome of AP has been addressed in multiple studies. Some recent studies have found that alcohol has a more severe course with higher mortality compared to GS-related pancreatitis.^{18,19} Still further, few studies highlighted that the outcome of HTG-related AP has a more severe outcome.²⁰

This study is conducted in a tertiary care center where a large number of patients is referred, rather than present at the first time, hence leading to the possibility of a referral bias.

The study had a higher percentage of patients in the moderately severe and severe AP categories, and only 9.6% patients had mild AP. The detailed nature of the local complications, such as difference in the sites of necrosis and sites of collection, between the two groups needs to be studied.

CONCLUSION

In summary, the results of our study showed that the outcome of AP was mostly independent of the basic etiology of the disease, namely, alcohol or GS, and more so in the severe form of

the disease. The number of local complications tends to be slightly higher in the alcoholic AP group. Further nationwide studies are required to validate these findings.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

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REVIEW ARTICLE**CYSTIC FIBROSIS-ASSOCIATED LIVER DISEASE: A REVIEW ARTICLE**

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Article received on: 22-04-2020

Article accepted on: 09-12-2020

ABSTRACT

Cystic fibrosis-associated liver disease (CFLD) is an important aspect of cystic fibrosis (CF), which manifests with various signs and symptoms. Lack of specific examinations for CFLD have made the diagnostic process of the disease time-consuming, and the disease is often identified after severe progress. Finding the associations between the outcomes of

various clinical, biochemical, and sonography examinations could help specialists identify the disease in a timely manner. This review study aimed to determine the correlations between the outcomes of various diagnostic approaches based on the current literature. According to the literature, some studies have reported correlations between various diagnostic approaches, while other studies have reported no associations in this regard. This discrepancy could be due to the various manifestations associated with CF.

INTRODUCTION

Cystic fibrosis (CF) is the nearly prevalent life-shortening, autosomal, recessive disease in a number of areas across the world, such as the United States, Europe, and Australia. The incidence of CF has been reported to be 1:3,500 live births^(1,2). Currently, the life expectancy of CF patients has bigger to further than 40 living in developing countries owed to the increase

in the management of the disease⁽³⁾. However, CF is nevertheless coupled with compound complications, such as hepatic cirrhosis, pulmonary failure, diabetes, and osteoporosis. amongst different complications of CF, liver disease is measured of great magnitude anticipated to its climax commonness and lay bare of mortality⁽⁴⁾. According to the definition by North America, cystic fibrosis-associated liver disease (CFLD) is indicated by the presence of liver cirrhosis and portal hypertension, persistent elevated liver enzymes, fibrosis, steatosis, and abnormal changes in ultrasound patterns^(5,6). The comprehensive global prevalence of CFLD has been reported to be 37.9%. According to statistics, approximately 2.5% of the global mortality in the patients with CF is connected with liver disease, which is notorious as the third leading cause of loss of life in these patients⁽⁷⁾.

To date, liver biopsy has been the nearly gold

Article Citation:

Kumar P, cystic fibrosis-associated liver disease. JIMC.2020;3(2): 41-45

standard technique for the assessment of CFLD. However, this technique enveloping and irregularly leads to difficult complications in the patients⁽⁸⁾. Among a choice of diagnostic methods, non-invasive techniques for the diagnosis and management of CFLD control attracted the concentration of specialists. Furthermore, early diagnosis of CFLD is of paramount importance due to the possible positive effects of ursodeoxycholic acid therapy, and there is an urgent need for the development of the trial of its prophylactic use. Some of the routine procedures for the diagnosis of CFLD include determining the clinical characteristics, biochemical tests, and sonography. Evidently, finding a rational correlation between various assessments could further support the early detection of CFLD.

This review study aimed to present the results of previous studies regarding the correlations between the outcomes of various diagnostic approaches for CFLD.

LITERATURE REVIEW

Clinical Features of CFLD

Detection of CFLD is challenging since it is a lot a subclinical disease and manifests with a broad form of signs and symptoms. The clinical appearance of CFLD might refrain from specialists to suspicious the disease and prescribe additional examinations for the patients in succession to bear out the diagnosis (10). In a study, Lamireau et al. exhibit demonstrated that CFLD is further shared in younger family (prevalence: 41%) at the period of 12 years. Similarly, Colombo et al. reported that the incidence time of liver disease is top in the patients with the history of meconium ileus, male patients, and individuals with severe genotypes .

In genotypes, factors such as pancreatic insufficiency and severity of pulmonary disease come up with been reported to begin CFLD. In a analysis conducted on 288 patients with CF, 256 had pancreatic insufficiency, and approximately one-third of these patients (n=80) were diagnosed with liver disease. some studies well described the other manifestations of CFLD, including portal hypertension, neonatal cholestasis steatosis, elevation of liver transaminases, lack of alkalization, and bile dehydration.

In this regard, the findings of Corbett indicated growth retardation and poor nutrition status importance in the patients with CFLD (13). Furthermore, factors such as the history of jaundice, changes in the stool pattern/ colour, abdominal pain, loss of weight, and family history of liver diseases must be careful in the patients with high levels of liver aminotransferases who are the possibility family history of liver diseases⁽¹²⁾. According to the examine by Ciuca et al., evaluation for portal hypertension, liver cirrhosis, and pancreatic insufficiency supposed to be measured as the first assessment of CFLD.

Diagnosis of CFLD

Biochemical Test

The serum assessment of transaminases is the most common test performed for the diagnosis of liver disease. However, the distance from the ground of liver enzyme levels is everyday in the patients with CF, therefore that it would not be linked with strict liver disease in every single one the cases.

Liver function test (LFT) was investigated in a group prospective study in this regard. According to the obtained results, approximately

25% of the patients had abnormal LFT, and in single 13% of the cases, a large overtone was experiential between high-minded LFT and clinical outcomes .

In a further research, Lindblad et al. assessed the pathological morphology of liver biopsies in quite a lot of patients, and barely a slender rise was practical in their serum transaminase levels . On the other hand, a variety of consider cover indicated that children with CF, who were exaggerated by multilobular biliary cirrhosis and rigorous fibrosis, had typical elevation of liver enzymes .

In a another research conducted by Williams during a nine-year period, the authors reported that the consequences of biomarker tests differed from sonography findings, and no correlations were experiential in this regard. In addition, in 3% of the patients with persisting abnormalities of the liver echo surface and persisting splenomegaly, the intensity of aspartate aminotransferase were inside the common range. In the mentioned study, 725 ultrasound examinations were performed .

Ling et al. followed-up 124 patients with CF for the substantiation of liver disease for four existence ⁽¹⁷⁾. According to the findings, 40% of the patients with abnormal clinical or ultrasound examinations had biochemically augmented aminotransferase levels. During the stick to up, 48% of the patients were practical to cover liver abnormalities in the clinical, biochemical, and ultrasound examinations. several of the before studies in this observe state furthermore definite the correlation between ultrasonographic findings in the patients with CF with their clinical and biochemical characteristics ⁽¹⁸⁾. Overall, Ling concluded that ultrasound and the

clinical examination of abnormalities based on biochemical tests might outcome in the induce identification of CF in the patients .

ULTRASONOGRAPHY

Ultrasound is a non-invasive, cost-effective, and exceedingly useful procedure for the diagnosis of hepatic steatosis, cirrhosis, and the complications caused by portal hypertension (e.g., ascites and splenomegaly). However, ultrasound cannot reliably rule out early on liver disease ⁽²⁰⁾.

According to the study by Leung et al., sonography abnormalities were practical in 18% of the patients with pancreatic scarcity in CF. The findings of the mentioned examination are coherent with the contemporary copy in this regard. even though 3.3% of the patients with no data of liver disease (e.g., portal hypertension and thrombocytopenia) had cirrhosis based on their ultrasound results. This may well be exactly to the manifestation of cirrhosis initial in life. Furthermore, no correlations were reported between meconium ileus, malnutrition, deteriorated FEV1, and ultrasound results. However, Leung claimed that meconium ileus is the likely lay bare issue for a homoge.

an alternative investigate in this have to do with was conducted on an infant population, and the consequences demonstrated no major disparity between meconium ileus and enhancement of liver disease in the patients with CF ⁽²²⁾. Moreover, Colombo investigated 177 patients with CF with a 14-year follow-up. According to the consequences of the mentioned study, the ultrasonographic patterns of 10% of the gear showed the presence of cirrhosis, bit near was

no sign of portal hypertensions .

In another study performed on 174 patients with CF, completely were followed-up every day for clinical, biochemical, and ultrasonography results. According to the findings, three children's develops CFLD during infancy, all along with the signs of portal hypertension. The outcome of ultrasonography also confirmed the progression of portal hypertension. According to the literature, multilobular cirrhosis with the development of portal hypertension is a most important liver disease in the patients with CF .

CONCLUSION

liver abnormalities has been reported in several of the patients with CF with normal biomarkers, as many studies be inflicted with demonstrated that the improper functions of the liver was evident in the clinical, biochemical, and ultrasound assessments of these patients. The discrepancies between the findings may possibly be owed to the varied assortment of liver disease manifestations, which may have an advantage to a variety of fallout in unusual investigations.

With respect to ultrasonography, a correlation has been reported between ultrasound patterns and clinical data in some studies, while other studies have denoted no such association. In fact, the correlations of various clinical symptoms have been reported variably in different studies. To obtain better results, it is suggested that specific research be conducted independently on the prevalent types of liver diseases to determine the correlations between various assessments.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

AUTHORS' CONTRIBUTION

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LETTER TO EDITOR**Urinary Tract Imaging in Children Post UTI**

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Letter to Editor received on: 07-07-2020**Letter to Editor accepted on:** 19-11-2020

Urinary Tract Infections (UTI) are common in children and radiologic imaging of the urinary tract is important to exclude structural abnormalities⁽¹⁾. Numerous international guidelines exist although follow-up imaging recommendations vary. These include repeat renal ultrasound (RUSS), Micturitioncystourethogram (MCUG) and/or Dimercaptosuccinic acid scintigraphy (DMSA)²⁻⁴.

The aim of this study was to review the radiologic imaging of children presenting with UTI and examine whether our data supports follow-up imaging as recommended in the guidelines. A retrospective chart review of all children admitted with UTI over a two-year period was conducted.

UTI was defined as a child with typical symptoms and a pure growth of an organism with a colony count >10⁵ on mid-stream urine culture.⁴ Atypical and recurrent UTI were defined as per NICE guidelines.²

A total of 241 cases were reviewed, mean (SD) age 25.19 (34.78) months. In these 241 patients, 217 (90 %) had UTI due to *Escherichia coli* and 47 (19.5%) had recurrent UTI. Acute RUSS was reported normal in 173/241 (71.8%), pyelonephritis was identified in 21 (8.7%) and other abnormalities in 39 (16.2%). Of 241

patients, 170 underwent follow - up RUSS, which was reported normal in 136 (80%) and abnormal in 34 (20%). DMSA was performed in 63 patients, of whom 46 (73%) and 17 (27%) experienced normal and abnormal DMSA, respectively. Moreover, 27 had MCUG, which was normal in 9 (33%) and abnormal in 18 patients (67%).

A significant association was observed between recurrent UTI and abnormal DMSA or MCUG in all age groups (p-value 0.01 and 0.03, respectively). Moreover, atypical UTI has an impact on the abnormal DMSA or MCUG in patients aged < two years (p-value 0.02 or 0.04, respectively), however the number of patients aged more than two years with atypical UTI was too small to draw a conclusion. A link was observed between the results of acute RUSS and DMSA or MCUG results. A total of 55 patients had both an acute RUSS and follow-

Article Citation:

Baloch F, Urinary Tract Imaging in Children Post UTI. JIMC. 2020; 3(2): 46-47

up DMSA, these were reported as abnormal in 27/55 (49.1%) and 12/55 (21.8%), respectively. Of 12 patients with abnormal DMSA findings, 8 (66.7%) also had an abnormal acute RUSS, with a statistically significant association between abnormal acute RUSS and abnormal DMSA (p-value 0.006).

A total of 27 patients had both an acute RUSS and follow-up MCUG, these were reported abnormal in 21/27 (77.8%) and 18/27 (66.7%), respectively. Of these 18 patients with abnormal MCUG findings, 17 had an abnormal acute RUSS, with a statistically significant association between abnormal acute RUSS and abnormal MCUG (p-value 0.011). Notably, the patients' age, gender or length of stay has no impact on radiological imaging abnormalities (p value >0.05). In children with UTI, follow-up imaging is important to identify those with renal scarring and/or VUR, particularly in children with recurrent or atypical UTIs and in those with abnormal RUSS. These results highlight the importance of following current guidelines regarding renal tract imaging following UTI in children.

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CONFLICT OF INCIDENCE

No conflict of interest declared by the authors.

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FB - Manuscript Writing



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