PREVALENCE OF THROMBOCYTOPENIA AND PANCYTOPENIA IN PATIENTS WITH MEGALOBlastic ANAEMIA

Shilpi Sikarwar¹, Ajay Pal Singh²

¹Assistant Professor, Department of Pathology, G. R. Medical College, Gwalior, Madhya Pradesh, India.

²Professor, Department of Medicine, G. R. Medical College, Gwalior, Madhya Pradesh, India.

ABSTRACT

BACKGROUND

Anaemia is a very common problem encountered by clinicians in Gwalior region. The incidence of megaloblastic anaemias is increasing. Megaloblastic anaemias are characterized by defective synthesis of Deoxyribo-Nucleic Acid (DNA) in all proliferating cells. They most commonly result from lack of folic acid or vitamin B12. In severe megaloblastic anaemia, thrombocytopenia and leucopaenia is usual. Thrombocytopenia and pancytopenia can lead to serious life-threatening illnesses including bone marrow hypoplasia. Severity and the underlying pathology determine the management and prognosis. The aim of this study was to evaluate out the prevalence of thrombocytopenia and pancytopenia in patients with megaloblastic anaemia (MA).

MATERIALS AND METHODS

A total 306 patients with MA were studied in the Department of Pathology, G.R. Medical College, Gwalior from May 2016 to April 2017. Demographic parameters including age and gender were recorded using preapproved proforma. Two blood samples were obtained from each patient to analyse thrombocytopenia and pancytopenia. All the data was analysed using SPSS Ver. 20 software.

RESULTS

Mean age of study cohort was 28.56±9.76 years with female preponderance. Most common age groups were 21-30 years (5163%). Prevalence of thrombocytopenia and pancytopenia in patients with MA was 46.60% and 17.32% respectively.

CONCLUSION

The prevalence of thrombocytopenia and pancytopenia is high. An early intervention is required to decrease the associated complications.

KEY WORDS

Megaloblastic Anaemia, Thrombocytopenia, Pancytopenia, Prevalence.

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BACKGROUND

Anaemia is a very common problem encountered by clinicians in Gwalior region. The high prevalence of anaemia is a serious health problem for the economic development and productivity of the country.

It has been found that incidence of megaloblastic anaemia is increasing over last two decades. MA occurs due to deficiency of folic acid and impaired absorption of vitamin B12. (Moghadam S, 2016)¹

Vitamin B12 deficiency is most frequently result from defective absorption of vitamin, while folate deficiency is most commonly due to inadequate dietary intake.

About 3 to 5 years are required for development of vitamin B12 deficiency after abrupt cessation of availability of vitamin B12; for folate deficiency this period is about 3 to 4 months.

This time interval is related to the daily requirement and the size of the storage compartment. Severe deficiency of vitamin B12 can result secondarily in decreased absorption of folate and vice versa. This is so because severe lack of either folate or vitamin B12 is associated with atrophy of rapidly dividing small intestinal epithelial cells and malabsorption.

Vitamin B12 deficiency is more common now a days, due to vegetarian life style of people. Food of animal origin (e.g. meat, eggs and milk) are the primary dietary sources. The amount of cobalamin intake is usually more than sufficient to meet normal requirement.

The major etiological factors of folate deficiency in tropical countries is inadequate intake of green leafy vegetables and animal proteins. Folate deficiency is very common in alcoholics. Alcohol interferes with metabolism and probably absorption of folate.

Pancytopenia and thrombocytopenia are routinely reported in patients with megaloblastic anaemias (MA) which is a group of hematologic disorders caused by abnormal DNA synthesis. Pancytopenia is an important clinic-haematological entity commonly encountered in severe megaloblastic anaemia. Pancytopenia is a disorder in which all three forms of blood components including red blood cells, white blood cells and platelets are decreased. (Ishtiaq O 2017)² Several diseases affect the production of all these cells by bone marrow which can result in to pancytopenia that means coincident presence of anaemia, leucopenia, and

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Corresponding Author:

Ajay Pal Singh,

#51, Maharana Pratap Nagar,

Near Usha Colony,

Gwalior-474001,

Madhya Pradesh, India.

E-mail: drajaypalsingh4@rediffmail.com

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thrombocytopenia. (Garg AK)³ It is not a disease, but a triad of finding that may occur from many disease processes involving bone marrow. (Gayathri BN 2011)⁴ Pancytopenia may result from number of disease processes – primarily or secondarily involving the bone marrow. The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patient.

Mild impairment in the bone marrow function may not be detected at early stage, but pancytopenia may become apparent only during time of stress or increased demand (e.g. bleeding or infection). As severity increases the peripheral blood count decreases even in the steady state. The basic investigation in the suspected cases of megaloblastic anaemia with pancytopenia include complete blood counts, peripheral blood film examination, reticulocyte count and cobalamin and folate assay. In peripheral blood film, blast cells may be evident in patients where pancytopenia is due to malignant infiltration. Neutrophils may show absent granulation and nuclear abnormalities suggestive of preleukemic or myelodysplastic states. In MDS cytopenia such as anaemia, neutropenia or thrombocytopenia, either singly or in combination is present in majority of patients. Hematopoietic dysplasia is characteristic of MDS. Bone marrow examination is indicated in all cases of pancytopenia, where underlying cause is not clear. This is particularly needed to exclude leukaemia or other malignant infiltration.

Several reports from world and India showed MA as the most common cause of pancytopenia and thrombocytopenia. (Kumar R, 2001⁵, Khunger JM 2002⁶, Santra G 2010⁷, Gayathri BN 2011⁴)

Megaloblastic anaemia and aplastic anaemia are important causes of pancytopenia in India. Since both may have presence of macrocytes, peripheral smear examination alone may pose a difficulty in distinction between the two in the absence of macro-ovalocytes and hypersegmented neutrophils, in these cases bone marrow examination is useful.

In megaloblastic anaemia, deficiency of either folate or vitamin B12 is associated with increased levels of homocysteine in blood. Hyperhomocysteinaemia has been linked with increased risk of thrombosis. Severe nutritional deficiency of vitamin B12 or folate causes megaloblastic anaemia whereas milder deficiencies are associated with increased cardiovascular risk. Insufficient folate during early pregnancy is implicated in the development of neural tube defects in the foetus.

Thrombocytopenia and pancytopenia, if left untreated can contribute to haemorrhagic complications. Thrombocytopenia many a times is the first sign of infectious diseases, hematologic malignancies and autoimmune disorders. (Izak M, 2014)⁸

Literature describing the prevalence of thrombocytopenia and pancytopenia in Indian population is limited; hence present study was performed to find out the prevalence of both the condition in Indian population.

MATERIALS AND METHODS

The present descriptive study was performed on 306 patients with MA who were enrolled consecutively in the Department of Pathology, G.R. Medical College, Gwalior from May 2016 to March 2017.

Institutional Ethics Committee approval and written informed consent from each subject was obtained before starting the study.

MA was diagnosed if e MCV is over 110 fL and hemoglobin, RBC count, WBC and platelets are decreased below normal. (Harrison Internal Medicine 18th Edition)

Thrombocytopenia is defined as if the complete blood count is fewer than 150,000 platelets. (Mayo Clinic)

Pancytopenia is a medical condition in which there is a reduction in the number of red and white blood cells, as well as platelets-

1. **Anaemia:** Hemoglobin < 13.5 g/dL (male) or 12 g/dL (Female).
2. **Leukopenia:** Total white cell count < 4.0 x 10⁹/L. Decrease in all types of white blood cells (revealed by doing a differential count)
3. **Thrombocytopenia:** Platelet count < 150x10⁹/L.

A preapproved proforma was used to document demographic data such as age and gender. With informed consent, two blood samples were collected from each patient, 2 ml in EDTA for complete blood counts (CBC) and 5 ml clotted blood for serum. CBC was done on the day of blood sampling.

All the data were analysed using IBM SPSS Ver. 20 software. Data is expressed as mean ± standard deviation (SD).

RESULTS

Mean age of study population was 28.56±9.76 years. Maximum patients belong to age group of 21-30 years [158 (51.63%)] followed by 31-40 years [75 (24.50%)]. Maximum subjects were female [167 (54.57%)] compared to male [139 (45.43%)].

Out of 306 subjects, 142 (46.40%) were found to have thrombocytopenia whereas 53 (17.32%) patients were having pancytopenia.

Prevalence of thrombocytopenia in patients with MA was 46.40% and prevalence of pancytopenia in patients with MA was 17.32%.

DISCUSSION

Megaloblastic anaemia most commonly results from folate or cobalamin (Vitamin B12) deficiency. It is a macrocytic anaemia that is usually accompanied by leukopenia and thrombocytopenia and specific bone marrow morphology affecting erythroid myeloid and platelet precursor.

Thrombocytopenia and leukopenia is more marked in severe megaloblastic anaemia. Pancytopenia is common haematological entity. It is a common feature of many serious and life-threatening illnesses that can range from simple drug induced bone marrow hypoplasia, megaloblastic anaemia to fatal bone marrow aplasias and leukaemias.

Most of the patient have the history of poor eating habits and many patients are of low-socioeconomic status. The high prevalence of nutritional anaemias in India has been cited for the increased frequency of megaloblastic anaemia.

Other common causes of pancytopenia is aplastic anaemia. Aplastic anaemia is more common in orient than western world which may be related to environmental factors such as increased exposure to toxic chemicals. Frequent use of drugs and chemicals are commonly

associated with aplastic anaemia. In agricultural country like India pesticide may be an important factor in high incidence of aplastic anaemia.

Some cases of pancytopenias are associated with acute leukaemia in our study. Aleukemic leukaemia, AIDS, hypersplenism, lymphoma can be associated with pancytopenia. But in this study, we have only taken the megaloblastic anaemia with cytopenia that is bilineage or trilineage.

Present study was performed to find out the prevalence of thrombocytopenia and pancytopenia in patients with MA. Results revealed that prevalence of thrombocytopenia (46.40%) was high whereas prevalence of pancytopenia was lower (17.32%). Female were more suffered from both the diseases compared to men.

Prevalence of thrombocytopenia reported by Matthews⁹ from UK was 6.3% which is much lower than the prevalence revealed by present study (46.40%).

Incidence of MA in India is high as reported by several Indian studies. (Gayathri BN 2011)⁴ And several studies have stressed upon the importance of MA in causing pancytopenia. (Tilak V 1992¹⁰, Kumar R 2001¹⁵) Several reports showed that aplastic anaemia is the main cause of pancytopenia worldwide but in Indian population MA is the main culprit. (Garg AK)³

Khattak et al¹¹ studied 90 patients to characterize of pancytopenia in MA and reported similar mean age with male preponderance, contrary to that in present study female patients dominated. Contrary to present study, study done by Prasad et al¹² and Reddy et al¹³ also reported male preponderance. Whereas study done by Agrawal et al¹⁴ and Kumar DB et al¹⁵ reported female preponderance.

In our study prevalence of pancytopenia in MA was 17.32%. Contrary to that higher prevalence was reported by Khattak et al¹¹ (70%), Zlotkin¹⁶ (68%) and Hamid et al¹⁷ (72%).

Clinical presentation and other demographic parameters were not studied in present study; a large clinical trial is required to strengthen the present study results.

CONCLUSION

In megaloblastic anaemia, thrombocytopenia and pancytopenia are common. It is an important clinical and haematological problem. A large number of patients with pancytopenia on initial investigations were later diagnosed to be suffering from megaloblastic anaemia. There is increased worldwide concern about the consequences of folic acid and vitamin B12 deficiency on health which include megaloblastic anaemia. Dietary deficiency of vitamin B12 due to vegetarianism is increasing. It also causes hyperhomocysteinaemia, which increases the risk of thrombosis. Thus, vitamin B12 deficiency having vague or highly variable presentation, can lead to many complications in the human body which can prove fatal if not diagnosed in time or left-untreated.

Physicians should have a high index of suspicion for vitamin B12 deficiency when dealing with patients presenting with symptoms of anaemia such as pallor and

weakness or diagnosed with pancytopenia on haematological examination.

Clinical findings along with haematological analysis are very important for the early diagnosis of both the diseases in order to start early intervention, so that survival rates may be increased.

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