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Incidence, Pattern and Characterization of Immune Thrombocytopenic Purpura

Medical Science

KEYWORDS : Immune thrombocytopenic purpura, Incidence, primary immune thrombocytopenia, secondary thrombocytopenia, ITP

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ABSTRACT

INTRODUCTION: Immune thrombocytopenic purpura (ITP) is a relatively uncommon disorder of acquired immune mechanism. Due to lack of adequate relevant data in India pertaining to incidence of immune thrombocytopenic purpura, designing of suitable clinical models and health resource allocation has become a little abstract and demanding. Knowledge of epidemiology and pattern of immune thrombocytopenia purpura is essential for devising new clinical trials and management of the condition.

OBJECTIVES: The objective of the present study is to determine the incidence, pattern and characterization by analyzing the data of routine haematological investigations in haematology laboratory of a tertiary care hospital.

METHODS: The present study is to determine the incidence and pattern of immune thrombocytopenic purpura by analyzing data of routine haematological investigations on the blood samples received in haematology laboratory of a tertiary care hospital located in peripheral area of Navi Mumbai with a mixed semi-urban and rural populations of diverse ethnic and socio-economic backgrounds.

RESULTS: In the present study, a total of 206 cases of immune thrombocytopenic purpura (ITP) are diagnosed by analyzing the data of haematological investigations of blood samples of 17,620 patients. Out of 206 (1.16%) cases of immune thrombocytopenic purpura, 138 (67%) cases are males and 68 (33%) cases are females. In the study, 24 (11.6%) cases are children, while 182 (88.3%) of cases occurred in patients over 12 years of age. 13 (6.3%) cases are known cases of ITP, while 193 (93.7%) cases are associated with other clinical conditions. In the current study, ITP is associated with 71 (34.4%) cases of Malaria and 35 (17%) cases of Dengue.

CONCLUSION: The present study shows an overall increased incidence of ITP based on analysis of database of routine haematological investigations carried out on blood samples of patients received in haematology laboratory of a tertiary care hospital. The study shows an increased incidence of ITP in adults than in children and also an increased incidence of ITP in males than in females. The overall increased incidence of ITP could be due to increased incidence causes of ITP such as co-existence of Malaria, which forms one-third of all the cases of ITP in the present study, Dengue and other clinical conditions such as alcoholic liver disease, malignancies and other conditions such as bacterial and viral infections and non-infectious conditions and their drug therapy that could collectively have led to secondary ITP.

INTRODUCTION

Immune thrombocytopenic purpura (ITP) is a relatively uncommon acquired autoimmune disorder characterized by isolated thrombocytopenia with no apparent alternative causative factors. There is marked paucity of statistical information on the prevalence of immune thrombocytopenic purpura in India. It is also true of relative lack of data on immune thrombocytopenic purpura in international literature. Thrombocytopenia is defined as platelet count less than 150×10^9/L and sometimes indicated as less than 100×10^9/L. However, it is considered severe if the platelet count is below 30×10^9/L, moderate if it is between 30×10^9/L and 50×10^9/L and mild (usually asymptomatic) if above 50×10^9/L[1]. Primary immune thrombocytopenic purpura (ITP) or autoimmune thrombocytopenic purpura, also known as idiopathic thrombocytopenic purpura, is defined as isolated thrombocytopenia in the absence of other causes with bone marrow being normal. Immune thrombocytopenic purpura is a clinical condition characterized by life-threatening bleeding episodes, the severity of which depend on the number of circulating platelets. There are exceedingly little data on the incidence and prevalence of immune thrombocytopenic purpura part of typographic error. in the United States of America (USA)[2]. The prevalence of immune thrombocytopenic purpura has been found to be 0.46 to 12.5/100 000 person-years in children and 1.6 to 3.9/100 000 person-years in adults [3]. In France, the prevalence rate of immune thrombocytopenic purpura was found to be 2.92/100 000 person-years (95% CI:2.83-3.01)[4]. In India too paucity of information on immune thrombocytopenic purpura makes the task of designing of health care resources for the study and management of the condition challenging. The objective of the present study is to determine the incidence of immune thrombocytopenic purpura by analyzing the haematological data in a tertiary care hospital.

OBJECTIVES

The objectives of this study is to determine the incidence and pattern of immune thrombocytopenic purpura (ITP) with an attempt at its characterization by analyzing the data of routine haematological investigations including platelet count available at the haematology section of the central clinical laboratory of a tertiary care hospital located in peripheral area of Navi Mumbai with a mixed semi-urban and rural populations of diverse ethnic and socio-economic backgrounds.

METHODS

The present study is to determine the incidence and pattern of immune thrombocytopenic purpura (ITP) by analyzing data of the routine haematological investigations such as complete blood count (CBC) on blood samples received in Haematology section of the central clinical laboratory, MGM's Medical College Hospital, Kamothe, Navi Mumbai. Blood samples were received in the laboratory as per National Bureau of Accreditation of Laboratories (NABL) guidelines. The cases of immune thrombocytopenic purpura are selected after analysis of 17,620 consecutive blood samples from both outpatients and inpatients received in the haematology laboratory. The blood samples were ana-

lyzed as per the NABL guidelines by using the standardized and calibrated automated haematology cell counters. Wherever the results of haematological analysis were ambiguous, repeat blood samples were collected to ascertain the findings. Pertinent information on patient demographics on all blood samples thus received was diligently collected.

NOMENCLATURE AND DEFINITION

For the sake of clarity of understanding, it is decided to use standard terminology and definitions in the current study as per the guidelines of International working Group (IWG) on immune thrombocytopenic purpura (ITP). Immune thrombocytopenic purpura, which is mostly represented by extensively used abbreviation, ITP, has been defined in variable ways as "immune thrombocytopenic purpura," "idiopathic thrombocytopenic purpura," and, most recently, "immune thrombocytopenia", the latter term being recommended as most of these conditions may not uniformly present with clinical features of purpura or bleeding disorders (Table 1) [5, 6]. In this scheme, primary ITP is defined as thrombocytopenia (platelet count < 100×10^9/L) occurring in isolation in the absence of other causes or disorders that may be associated with thrombocytopenia. Secondary ITP is defined as a type of immune thrombocytopenia which occurs in the backdrop of presence of other conditions such as systemic lupus erythematosus, hepatitis C infection or lymphoproliferative disorders. The term "acute ITP" is replaced by the term "newly-diagnosed ITP", which refers to ITP diagnosed within the preceding 3 months. Immune thrombocytopenia that occurs between 3-12 months duration is designated as "persistent ITP", while "chronic ITP" is defined as disease of more than 12 months duration. The term "Severe ITP" is used to indicate the presence of bleeding symptoms at presentation, or the development of new bleeding symptoms while on therapy, which might mandate additional clinical intervention. "Refractory ITP" is the term used to denote cases of immune thrombocytopenia that have not responded to splenectomy or have relapsed thereafter, and are severe in clinical manifestations with possible impending risk of bleeding to require ongoing therapy.

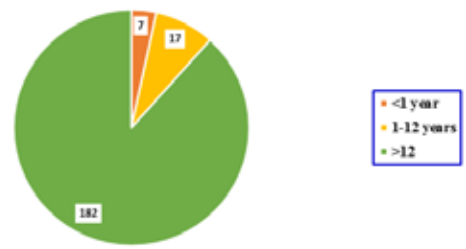
Table 1. Proposed definitions by International Working Group (IWG) on immune thrombocytopenia

PRIMARY ITP	An autoimmune disorder characterized by isolated thrombocytopenia (platelet count < 100×10^9/L) in the absence of other causes and disorders that may be associated with thrombocytopenia. The diagnosis of primary ITP is made by exclusion, since no clinical or laboratory means or parameters are available to diagnose the condition with accuracy. The most clinical risk in cases of primary ITP is an increased risk of bleeding, albeit bleeding symptoms are infrequently present.
SECONDARY ITP	All forms of immune-mediated thrombocytopenia other than primary ITP. The acronym ITP should be followed by the name of the associated disease, (e.g. secondary ITP-lupus associated, secondary ITP-drug induced)
PHASES OF ITP	Newly diagnosed ITP: ITP within 3 months of diagnosis
	Persistent ITP: ITP occurring between 3-12 months. It includes patients not reaching spontaneous remission or not maintaining complete response off therapy.
	Chronic ITP: ITP lasting for more than 12 months
	Severe ITP: presence of bleeding symptoms at presentation sufficient to mandate treatment, or occurrence of new bleeding symptoms requiring additional therapeutic intervention with a different platelet enhancing agent or an increased dose of an ongoing platelet enhancing agent.

RESULTS

In the present study, the data of routine haematological investigations such as complete blood count (CBC) of blood samples of 17,620 patients received in our institutional haematology laboratory is analyzed and a total number of 206 (1.16%) cases of immune thrombocytopenic purpura are diagnosed. Out of 206 cases diagnosed, 24 (11.6%) were children while 182 (88.3%) were adults **(Figure 1).**

FIGURE 1: AGE INCIDENCE OF ITP



It is also found that the 7 (3.3%) cases of ITP occurred in children below one year of age, while 17 (8.2%) cases of ITP occurred in children between one and twelve years. In the present study, males formed bulk of the patients and comprised 138 (67%) out of a total of 206 cases and the number of females patients is 68 (33%). Most of the conditions for which the analysis of blood samples of the patients is carried out in the current study are mostly related to clinical conditions other than immune thrombocytopenia except 13 (6.3%) known cases of thrombocytopenia. In a total of 206 cases of diagnosed ITP, 71 (34.4%) cases are of malaria and 35 (17%) cases of Dengue, both associated with secondary thrombocytopenia. In the present study, 11 (5.2%) cases are of alcoholic liver disease; 9 (4.3%) cases are diagnosed in patients admitted with clinical history of road traffic accidents and 8 (3.8%) have been known cases of malignancy, while 58 (28%) cases belonged 'others' category of clinical conditions, not directly associated with thrombocytopenia **(Table 2)**.

Table 2: Diseases for which blood samples analyzed leading to diagnosis of ITP

SERIAL NUMBER	DISEASE	NUMBER OF CASES	PERCENTAGE (N=206)
1.	Malaria	71	34.4%
2.	Dengue	35	17%
3.	ITP (known cases)	13	6.3%
4.	Alcoholic liver disease	11	5.2%
5.	Road traffic accident (RTA)	9	4.3%
6.	Malignancy	8	3.8%
7.	Others	58	28%

Out of 206 cases of ITP detected, 13 (6.3%) cases of ITP were previously diagnosed and confirmed cases of ITP and their blood samples were received for routine monitoring of therapy and prognosis and hence are considered as primary thrombocytopenic purpura. The clinical features were not pronounced in most of the cases of ITP except for the cases of neonatal thrombocytopenia which were already on therapy and had history of presenting with purpura when patients had visited the hospital in the initial stages of treatment. The platelet count of all the 7 (3.3%) cases of

neonatal thrombocytopenia was inconstant and varied periodically from $17x10^9$/L to $150x10^9$/L, while 13 (6.3%) known cases of ITP were also undergoing therapy and their platelet count was not constant and varied between $63x10^9$/L to $150x10^9$/L.

DISCUSSION

In the present study, we have analyzed the data of routine haematological investigations of patients visiting our hospital located in an area with a composite semi-urban and rural population of diverse ethnic and socio-economic backgrounds. The data of routine haematological investigations such as complete blood count including platelet count of 17,620 patients, both outpatients and inpatients, was analyzed to determine the number of cases of immune thrombocytopenic purpura. In the present study the overall incidence of ITP is 206 (1.16%) out of a total of 17,620 patients. In a nation-wide study conducted in France by Guillaume Moulis et al [4], the incidence of ITP was 2.9/100,000 person-years. J. B. Segal and N. R. Powe[2], in their study in the USA, found the incidence of ITP to be 9.5 per 100,000 persons. In the current study, most of the cases of ITP were associated with other diseases **(Table 2)** and only 13 (6.3%) case are diagnosed as primary ITP, the incidence of which is very high compared to the findings of studies conducted in Oklahoma by Deirdra R. Terrell et al[7] which was 11.2 (95% CI 10.4, 12.0) per 100,000 population.

In our study, 7 (6.3%) cases of ITP are detected in children under one year of age and are considered as part of neonatal thrombocytopenias. Sonam S. Nandyal et al,[8] in a study conducted on neonates found 99 cases of neonatal ITP in 155 patients with an incidence of 63.8%. In Harcourt region of Nigeria, Zaccheaus A Jeremiah and Justina E Oburu[1] found in their study on neonatal ITP a prevalence rate of 53%. In the present study, 17 (8.2%) cases of ITP are found among children between the age of one and twelve years in a total of 206 cases of ITP. Sajedeh Saeidi et al[9] found a total 223 (69%) cases of ITP among children above one year out of a total of 323 cases in a study conducted in Iran.

In our study, 138 (77%) cases of ITP are males and 68 (33%) cases are females. Sajedeh Saeidi et al[9] reported a mild difference in the incidence of ITP between males (49.5%) and females (50.5%). Guillaume Moulis et al [4] found an incidence of 2.92 per 100,000 persons-year for males and 3.03 per 100,000 persons-year. Walter et al,[10] in their study on epidemiology of thrombocytopenia in Canada, showed that incidence of ITP in males and females is 41.5% and 58.5% respectively. Dimitri et al,[11] in a study conducted in UK, showed the incidence of ITP to be 40.6% in males and 59.4% in females.

In the present study, out of 206 cases of ITP, 193 (93.6%) cases are associated with other clinical conditions and only 13 (6.3%) cases are diagnosed as primary ITP. Among a total 206 cases of ITP, 71 (34.4%) cases are associated with Malaria. Prashant Patel et al[12] have studied a total of 1480 cases of Malaria and reported an incidence of ITP in 1161 (78%) cases. Similarly, Narendrakumar Gupta et al[13] reported an incidence of thrombocytopenia in 179 (77.8%) of ITP in a total of 230 cases of all types of Malaria. Saravu et al[14] reported an incidence of 46% and 54% of Plasmodium vivax and Plasmodium falciparum infection in 131 cases of Malaria studied with low platelet counts reported in almost all cases, but platelet count being severely low in complicated cases of Plasmodium falciparum.

In our study, the incidence of ITP is observed in all the 35 (17%) cases of Dengue. Alex Chairulfatah et al[15] reported thrombocytopenia in 1198 out 1300 cases of Dengue in Indonesia with an incidence of 92%. Mahendranath et al,[16] in their study of 85 cases of Dengue, reported mild thrombocytopenia in 53 cases and moderate thrombocytopenia in 29 cases with 100% overall incidence of thrombocytopenia in Dengue cases. Tamil Selvan et al[17] reported an incidence of 92% of thrombocytopenia in a study of 300 Dengue cases in Bengaluru.

In the present study, 11 cases of alcoholic liver disease are associated with thrombocytopenia, which form 5.2% of a total of 206 cases. According to the study conducted by S.H. Hancox and B.C. Smith,[18] thrombocytopenia was associated with 93% of chronic liver diseases including alcoholic liver disease, and according to Nezam Afdal et al,[19] 76% of chronic liver diseases are associated thrombocytopenia.

In our study, 8 (3.8%) cases are associated with known, previously diagnosed cases of malignancy and 9 (4.3%) cases were admitted with road traffic accidents involving musculoskeletal traumatic injury. Our study also comprised a large category of 58 (28%) cases of thrombocytopenia grouped under 'other' clinical cases which included routine clinical conditions of uncertain diagnosis such as upper respiratory tract infections, gastrointestinal infections, Diabetes mellitus, hypertensive heart disease and ischaemic heart disease and cerebrovascular disorders and cases without any specific history of illness. Some of these conditions could be cases of drug-induced thrombocytopenia as it is reported by Jessica A.Reese et al[20] that out of 253 drugs used in the treatment of many clinical conditions varying from infections to various malignancies, 87 (36%) were confirmed to be causing thrombocytopenia in varying degrees. Douglas B. Cines et al [21] also reported many drugs used in the treatment of viral and bacterial infections as well as various vaccines used for prophylactic management of infectious diseases are known to cause thrombocytopenia. Johansen ME and Jensen et al[22] have reported that antimicrobials cause thrombocytopenia in 18% of critically ill patients within 24 hours of admission to intensive care units followed by 57% of them developing thrombocytopenia during follow up.

CONCLUSION

The present study shows an overall incidence of ITP in patients, which is obtained after analyzing the database of routine haematological investigations in the haematology laboratory of a tertiary care hospital. The incidence of ITP is very high with 206 cases of ITP detected in a total of 17,620 patients whose blood samples were analyzed in our institutional haematology laboratory. In the present study, the incidence of ITP is found to be high in adults than in children and is also high in males than in females The overall incidence of ITP is high possibly due to an increased incidence of known causes of thrombocytopenia such as co-existence of Malaria, which form one-third of all cases in the present study, and other associated clinical conditions such as Dengue, chronic liver disease, malignancies and other clinical conditions including various bacterial and viral infections and non-infectious conditions and their drug therapy that could collectively have led to secondary immune thrombocytopenic purpura (ITP).

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