

IDIOPATHIC THROMBOCYTOPENIC PURPURA  
(I.T.P.)

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In a study of 3000 cases who had referred to the clinic of hematology, the department of hematology and also to departments of internal medicine at the Imam Khomeini Medical Centre during the years 1975 til 1983 except 1978, for "I.T.P. and the role of sex in this disease" with stress on sex, age, place of birth and place of residence of these patients, and statistical deductions of the above mentioned factors, we came to a conclusion which will be presented here for the benefit of those interested in studying this disease in Iran (together with the clinical course of the disease and its positive laboratory findings).

Here, a description of the disease itself, shall be followed by a discussion on the obtained results.

To our present knowledge, this disease has no specific cause. It may be seen at any age, but is generally more common amongst children and young adults. I.T.P. is seen in two forms: acute and chronic. Other names have been used for describing the signs and symptoms of the disease, all of which, represent I.T.P. These include:

Essential thrombocytopenia

Purpura Haemorrhagica

Werlhof's Disease

Primary thrombocytopenia

#### Acute I.T.P.

In this form, there is a sudden onset of the disease with signs such as hemorrhage in the skin and mucosae, which represents itself as petechiae and purpura (The hemorrhage is often spontaneous). Hemorrhage is mostly seen in the upper thorax and neck, arms and legs. This form of ITP is more seen in children and a point worth noticing is that in this form the disease is equally prevalent in both sexes. In a large number of reports, a history of an infection (especially upper respiratory tract infection), 2-4 weeks before the appearance of acute ITP's signs, has been stated.

Hemorrhage from the G.I. tract, gums, nose and even hematuria has been frequently seen as a result of mucosal involvement in this disease, and can be one of the early clinical manifestations of the disease. One of the

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most important laboratory findings in the course of this disease is the severe decrease in the platelet count, which can reach levels as low as 10,000 per mm<sup>3</sup>. Other findings are: prolonged bleeding time, impaired clot retraction, anemia and a relatively significant increase in the WBC count.

In the bone marrow study of these patients the essential point is the immaturity of the megakaryocytes which are unable to produce platelets.

Acute I.T.P., as evident from its name, runs an acute course, but is fortunately self-limiting and the disease subsides after two to three weeks from the onset. In this condition, two possibilities should be considered. One is that the disease may relapse again and the other is that around 25% of the cases may progress to the chronic variety of the disease.

#### Chronic I.T.P.:

The onset of this form of the disease is often insidious (except for the cases that result from the conversion of the acute form). Ecchymoses and especially menorrhagia in women are considered the best clues to clinical diagnosis

The possibility of being affected by this disease exists at all ages, but it seems that it is more prevalent among young adults. According to the various studies done on chronic I.T.P., It has become apparent that the females are affected 3-4 times more often than males. This fact is one the chief issues of study in the report you are about to see.

In addition to the dermal manifestations and menorrhagia, the first manifestation of the disease may follow

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an accident with traumatism, surgical procedures, or even the excision of a tooth.

According to the studies carried out, laboratory findings of chronic ITP are much the same as acute ITP except that it may be less severe. For example, the platelet count may be more than the acute form (ie 50,000 to 80,000 slightly more or less). In the patients that shall be presented here, the platelet count in the chronic form has often been below 50,000.

Generally, chronic ITP has a gradual and intermittent course ie the patient may be asymptomatic for a short or relatively long period of time, but occasionally it presents itself with bleeding from the sites previously mentioned.

It should be noted that according to international data, ITP is the most common cause of thrombocytopenic purpurae: slide 1, 2, 3, 4, 5 and 6.

#### Course of disease :

ITP is a syndrome as diverse as its clinical manifestations, so that its treatment cannot follow a rigid protocol. There are mild cases with minor hemorrhagic manifestations, and these may do well even without therapy. There are severe cases in which treatment must be prompt and aggressive.

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	Male	Female	Total
Number	21	43	64
Percent	32.8	67.2	100

Table 1. Incidence of ITP (acute or chronic) in two sexes for 3000 records.

	Acute Form	Chronic Form	Total
Number	5	59	64
Percent	7.8	92.2	100

Table 2. Incidence of the acute, chronic forms of ITP in our patients. (regardless of sex).

Every effort should be made to achieve a definitive diagnosis. It is not enough to define the presence of a thrombolytic process, immunologic in character (i.e. to establish the general diagnosis of ITP); one must try to ascertain whether the disease is truly idiopathic or secondary, acute or chronic. It is essential to ferret out any possible etiologic factor, including drugs, chemicals and recent infections, and to inquire about previous purpuric or hemorrhagic manifestations. The severity of ITP must be quickly evaluated, and hospitalization should be advised in most cases in which the purpura is widespread and bleeding from nose, gums, urinary tract and gastrointestinal tract is abundant, when the platelet count is below 20,000 per cu. mm. Purpura and other hemorrhagic symptoms are usually prominent and hospitalization is advised in most cases.

The age of the patient and the type of onset of the disease, besides the platelet count, have importance in determining the degree of risk and in defining the immediate prognosis. A child is less prone to spontaneous intracranial hemorrhage than an older person although traumatic hemorrhage is more common in children. An abrupt onset of the disease and the history of a preceding "viral" infection leading to the possible diagnosis of acute ITP should alert the physician to the possibility of a stormy course and to the need of immediate supportive therapy, particularly if the patient is advanced in age. Death from all cases of ITP is known to be limited, although recent useful statistics on this point are not available.

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In one experience, acute ITP in children leads to death in less than 1 per cent of patients.

However, acute ITP in old age may have a death rate of 20 to 40 per cent depending on the available supportive therapy and on the type of ITP, whether idiopathic or secondary to an infection or a drug. The latter is usually more severe than the former.

Chronic ITP is rarely accompanied by severe complications, in most patients. With proper management, the patients may still lead a useful life even with cases refractory to corticosteroids, splenectomy, or immuno-suppressive therapy. A patient with a platelet count above 20,000 per cu. mm. may even go through surgery without excessive risk, provided that platelet transfusions are given at the time of the operation.

Now it is important to know how is the prognosis of chronic ITP in adult women. ITP in pregnancy is not necessarily fatal and pregnancy in ITP is not an unsolvable problem. Thrombocytopenia, including ITP, does not cause sterility, although the rate of spontaneous abortion is about doubled. Toxemia of pregnancy is not aggravated by thrombocytopenia, although corticosteroids may indeed render it more severe. If we exclude patients with acute ITP, which is commonly severe in the adults, chronic ITP does not represent a high risk for the pregnant mother unless she is recklessly subjected to splenectomy.

In this event, premature labor and maternal death are frequent, and fetal death in the uterus occurs in about one fourth of the cases. Early as well as recent reviews concur that maternal mortality in chronic ITP is not

## Idiopathic Thrombocytopenic Purpura

Chronic Form	Female	Male	Total
Number	41	18	59
Age (Year)	16-60	17-49	16-60
Percent	64.1	28.1	92.2

Table 3. Prevalence of chronic ITP with respect to sex and age. (From the total of 64 patients with ITP, 59 of them were chronic, these have been the basis of this table).

(Based on this table, Male to Female ratio in chronic ITP is 1/2.3).

significantly higher than what could be expected from the ITP itself. Due to the increased corticoid excretion of the placenta, an improvement of the thrombocytopenia during pregnancy should be expected. This is, however, not the case. In this respect, Baldini's experience corresponds with that of Schenker and Polishuk. Especially during the third trimester of pregnancy, thrombocytopenia and purpuric manifestations often become more severe, probably due to the increase of placental and abdominal congestion and blood stagnation, and the physician may be forced to increase the dose of corticosteroids.

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Complications of ITP in pregnancy include premature separation of the placenta and premature labor. With the presently common availability of platelet transfusions, postpartum hemorrhage may be prevented in most cases. About 65 percent of the babies have thrombocytopenia at birth. This is caused by the passage of antiplatelet auto-antibodies across the placenta, but it lasts only 1 to 3 weeks. Fetal mortality ascribed to thrombocytopenia is less than 10 per cent.

#### Pathogenesis:

According to various world-wide studies on ITP, it seems that there is an immunological cause to the disease and a factor which acts through the blocking of thrombocytes has been blamed in the pathogenesis of the disease. This factor has been claimed to be an immunoglobulin.

Albert F. Lo Buglio reported Aug. 1983 in N. Eng. J. Med. about: 125 I - labeled antihuman Ig G monoclonal antibody to quantify platelet-bound Ig G. This technique can help us to differentiate between immune and nonimmune thrombocytopenia, according to clinical criteria, but one resistant to therapy, may be related to factors other than Ig G antibody.

Platelet antibodies are present in the plasma of most patients with ITP. For this reason the term autoimmune thrombocytopenia has been proposed. It is also known that transient thrombocytopenia may occur in infants born to mothers with ITP, suggesting transplacental passage of the antiplatelet factor. The antibody has been shown to be an Ig G which sensitizes platelets for sequestration by the spleen and liver. Following splenectomy, the liver may become the chief site for sequestration.

In other site, we can say antibody-mediated-thrombocytopenia may be due to auto-antibodies in idiopathic thrombocytopenic purpura. This auto-antibody is seen more in females than males. Therefor, it needs certain genetic studies.

There are 6 factors which support the immungenesis of ITP (Werlhof diseasis).

- 1) ITP occurs like to others autoimmun-diseases more in female sex.
- 2) Newborns from mothers with "ITP" involve about 60.
- 3) The survival time of platelets is markedly decreased from the normal of 10 days to less than 1 day, it is the same also for the platelets transfusion.
- 4) The auto-antibody is an immunglobulin (Ig G).
- 5) The spleen is one site to synthetize this auto-antibody.
- 6) Platelet antibodies can be demonstrated in vitro, but these tests are difficult to perform and are not yet part of routine laboratory studies.

Acute Form	Female	Male	Total
Number	2	3	5
Age (Year)	6-15	5-14	5-15
Percent	3.1	4.7	7.8

Table 4. Prevalence of acute ITP with respect to sex and age. (From the total of 64 patients with ITP, 5 of them were acute; these have been the basis of this table).

(Due to restricted number of acute ITP in this study, comparison seems impossible)

	Female	Male	
Number of patients with acute ITP	2	3	From the total of 64 patients, 5 have had the (7.8 % of total).
Percent of patients with acute ITP	3.1	4.7	Considering 64 patients 100 %, 7.8 % have been affected with acute form.
Number of patients with chronic ITP	41	18	From 64 patients with ITP, 59 have had the chronic form (92.2 %).
Percent of patients with chronic ITP	64.1	28.1	Considering 64 patients 100 %, 92.2 % have been affected with chronic form.

Table 5. Statistical comparison in the patients with ITP with respect to sex in acute & chronic forms of the disease.

(64 patients have been selected after the survey of 3000 records).

(From the total of 59 patients with chronic form of ITP, the number of female patients exceeds by 22 the male patients; in other words, the females have been affected 2.3 times more than males which is the result of this study).



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**Therapy:**

it has two cornerstones:

- (1)- Reducing the production of antibodies thought to be responsible of producing ITP.
  - (2)- Preventing the destruction of the previously sensitized platelets. The first can be achieved by using immunosuppressive drugs, the second by splenectomy.
- Corticosteroids interfere with both pathways and hence can be used in treatment.
  - Supportive therapy - When the patient has had an accident or is being prepared for surgery he will need active supportive therapy. This is best obtained by the use of platelet transfusions. Transfusions of fresh platelets are highly effective in the control of bleeding in ITP.

**Abstract :**

The course of the disorder is acute and chronic. The acute form of the disease occurs most commonly in children, but is seen in adults as well.

The chronic recurrent form occurs most often in women between twenty and forty years of age.

We have studied 3000 cases from the patients of hematological and internal department in Imam Khomainsi Medical Centre, Uni. of Tehran/IRAN.

We have found also the chronic disorder occurs about 70 % adult women.

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