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Chronic Idiopathic Thrombocytopenic Purpura (ITP) and its management through Unani system of medicine: A Case Study

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ABSTRACT:
ITP is an auto-immune disorder which is characterized by the production of auto-antibodies targeted toward platelets, in this event T-cells directly attack platelets. On the basis of clinical presentation, Idiopathic thrombocytopenic purpura is classified into acute and chronic forms in which severe bleeding, or insidious with slow development with mild or no symptoms occurs. Corticosteroids and intravenous immunoglobulins were the mainstay of immediate treatment after 1950s with splenectomy for more than 100 years remains the only option for treatment. Unani System of Medicine is based on the Concept of Humours i.e., *Nazariya-e-Akhlāt,*according to which the four *akhlāt* (*dam* (blood), *balgham*(phlegm), *safrā'* (yellow bile) and *sawdā')* are found mixed in right proportion in the body during the state of health but when there is dyscrasia, disequilibrium occurs in this proportion, the diseases arise. According to Unani System of Medicine, ITP is thought to be the disorder of *akhlāt* due to alteration in quality and quantity of normal blood components. Thus the mainstay of treatment of ITP in in Unani System of Medicine is focused on correcting the humoral imbalance and restoring the equilibrium.

KEYWORDS: Auto-antibodies, Corticosteroids, Humours, Heamatopoeisis, Immuunological disorders, Purpura.

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INTRODUCTION:

Idiopathic (or immune) thrombocytopenic purpura (ITP) is characterized by immunologic destruction of platelets and normal or increased megakaryocytes in the bone marrow.

Both acute and chronic form of ITP has different pathogenesis. Acute ITP is a self-limited disorder seen most frequently in children following recovery from a viral illness, or an upper respiratory illness. The onset of acute ITP is sudden and severe thrombocytopenia but recovery occurs within a few weeks to 6 months.[1]

Chronic ITP more commonly occurs in adults, particularly in women of childbearing age.

The etiology of chronic ITP is unknown but the pattern of thrombocytopenia associated with Systemic lupus erythematosus (SLE), an Acquired immunodeficiency syndrome

(AIDS), and autoimmune thyroiditis mimics the chronic ITP.

The pathogenesis of chronic ITP is explained by the formation of anti-platelets auto-antibodies, usually by platelets-associated IgG humoral antibodies, synthesized mainly in the spleen. These antibodies are directed against the target antigen on the platelet glycoproteins, Gp IIb-IIIa and GP Ib-IX complex. Some antibodies also interfere with their physiological functions. The destruction of platelets is similar to that seen in autoimmune hemolytic anemias. Sensitized platelets are destroyed mainly in the spleen and rendered susceptible to phagocytosis by cells of the reticuloendothelial system. [1]

In acute cases of ITP clinical manifestations develops rapidly but in chronic ITP, sign, and symptoms develop gradually. The usual manifestations are petechial hemorrhages, easy bruising, and mucosal bleeding such as menorrhagia in women, nasal bleeding, bleeding from gums, melaena, and haematuria. Intracranial hemorrhage is, however rare. Hepato-splenomegaly is found in most of the cases of chronic ITP but lymphadenopathy is uncommon in either type. ITP is usually treated with immunosuppressive therapy.[2] Corticosteroids and intravenous immunoglobulins were the mainstays of immediate treatment after the 1950s with splenectomy for more than 100 years remaining the only option with curative potential.

Unani Concept:

Unani System of Medicine (USM) has a unique concept of akhlāt (Dam, Balgham, Safra and Sauda) which are found in the body.

Humoural Theory of Hippocrates suggests that the body remains in the state of health when there is a balance maintained in all the four akhlāt (Humours) viz. dam (blood), balgham (phlegm), safrā' (yellow bile), and sawdā' (black bile) in the body. The diseases arise when there is any disequilibrium or dyscrasia in this proportion. [2],[3]

Abnormality arises in dam (blood) due to change in its normal composition. Alteration occurs both in quantity and quality both. There may be change in the physiological make-up of the blood or an alteration in physical characteristics such as viscosity or blood may itself become infected with toxins. If we correlate these abnormalities with the modern concept of blood diseases then all bleeding disorders and coagulopathy fall under decreased viscosity of blood. [4]

According to the interpretation of USM, ITP is a disease of akhlat, and akhlat are chiefly produced by the liver. Medical Science first became aware about the Thrombocytopenia in 19th century and platelet was identified as a leading component of the Idiopathic thrombocytopenic purpura (ITP). [5] Unani physicians hold the opinion that most of the metabolic functions take place in liver [6] and they knew that along with the liver other organs are also involved in the formation of blood. [7] Whereas modern medicine argues that various useful substances are formed in the liver that directly or indirectly controls the hematopoiesis. [8]

Northern blot analysis suggests that the liver and kidney are the principal sites of thrombopoietin (Tpo) mRNA expression and alteration in Tpo production may lead to a significant reduction in platelet levels. [9-10]

CASE REPORT:

A 28 year old male previously diagnosed with Chronic Thrombocytopenic Purpura was registered through the OPD of Central Research Institute of Unani Medicine, Basaha, Kursi Road, Lucknow. He came with the complaints of blood blisters in the

mouth, nasal bleeding, bleeding from gums and petechial hemorrhages on arms, chest and different part of the body and marked reduction in platelets counts which was shown by the investigation record since 2006. After taking the detailed history it was revealed that he was suffering from this ailment since 2006, and that he was relatively in good health except the bleeding problems and extreme fatigue. He had taken treatments from local physician. During the course he rushed Lucknow, India to consult a renowned physician and professor of Medicine & Haemato-oncologist. He diagnosed chronic Idiopathic thrombocytopenia purpura (ITP) since then he was under his treatment but could not get complete relief.

Since the patient was already diagnosed chronic ITP, and came along with the features of the chronic idiopathic thrombocytopenic purpura (ITP) the patient was registered and managed according to the three basic usool-e ilaaj (Principal of treatment) which are as follows:

A. Checking the Nazfal'dam (Hemorrhagic Condition)

B. Correction of Liver and spleen functions

C. Enhancing the Immunity of the patient

On the basis of above principles the patient was advised with following combination of Unani pharmacopeial formulations, selected and prescribed as, Sharbat Anjbar 20ml twice a day, Qurs Kushta Marjan Sada 2 tablets twice a day, Habb Zahar Mohra 2 pills thrice a day, Majun Dabeedul ward 10gram twice day in the empty stomach, Jawarish Jalinoos 5gram twice day, and a brand product Tehali10ml twice day after meals with plain water, selected as principal medicines. (Table no.1) Hence the goal of therapy was to correct the liver and spleen functions which directly or indirectly involve in the synthesis of clotting factors and the thrombocyte production.

History of present illness:

According to patient's statement, before August 2006 he got some hemorrhagic blisters in buccal mucosa and consulted local practitioners but did not get relief, since then he has been gradually progressing bleeding from gums and nose, blackish/bluish patches in arms, chest and different part of the body. He consulted to the doctors in Lucknow and they diagnosed as ITP. Since he went under treatment of different doctors and hospitals but could not relief completely.

H/o past illness:

The patient has no past history of Dengue, Malaria, HIV, Hepatitis etc.

Family History:

No any history of parent and siblings related to such type of complaint was found.

History of Treatment:

Patient was on corticosteroid medication since he was diagnosed and doctors had advised for spleenectomy.

Personal history:

Non vegetarian, Non alcoholic, non smoker and non tobacco chewer, appetite was normal, Bowel- non clear constipated, Bladder clear.

General Physical Examination:

Patient was a young short heighted male apparently healthy, his blood pressure was 120/80mmHg, Pulse Rate 79/min, Respiratory Rate 16/min. Temperature 98.4F. Pallor, icterus, cyanosis and clubbing of fingers not present and no any lymphadenopathy found. His skin was dry there was diffuse blackish/bluish patches on the arms and the upper trunk, and bloody lesions located on buccal mucosa and sublingual region.

Systemic Examination:

CNS: well conscious and Oriented. CVS: S1 S2 audible, Normal. RS: AEBE, Clear. Abdomen: tender on Rt. Hypochondric Region and liver was slightly palpable otherwise soft.

Laboratory Investigations:

All the biochemical and pathological investigations since August 2006 to August 2018 revealed that all the counts were within the normal limits except the platelet count which was markedly reduced i.e., 0.35Lac/cmm. Peripheral blood smear shows no any abnormal or immature cells. RBC, WBC was also apparently shown normal and there were no hemolysis. Platelets were normal but reduced in numbers. Coagulation parameters were within normal limit. C - reactive protein and Serum Uric acid were elevated but Rheumatoid factor is negative. The Renal Functions and thyroid were normal.

Bone marrow smears showed increased Megakaryocytes with normal morphology.

Table- 1: Medication Details:

Name of Formulation	Dosage	Timing	How to take
Sharbat Anjbar	10ml	BD	With plain water
Qurs Kushta Marjan Sada	2 tab	BD	With plain water
Habb Zahar Mohra	2 tab	TDS	With plain water
Majun Dabeedul ward	5 gram	B.D. Empty stomach	With plain water
JawarishJalinoos	5 gram	BD after meal	With plain water
Tehali	10ml	BD after meal	With plain water

Table-2: Subjective parameter:

Parameters	Before Treatment	After treatment
Fatigue	Present	Absent
Peticheal Haemorrhage	Present	Absent
Blood blisters in the mouth	Present	Absent
Nasal Bleeding	Present	Absent
Bleeding from Gums	Present	Absent
Malaena	Present	Absent
Splenomegaly	Present	Absent
Hepatomegaly	Present	Present

Showing improvement clinical parameter

Time Period 1 [TP-1]: 2006.10.27 to 2008.10.11

Time Period 2[TP-2]: 2012.02.10 to 2018.03.08

Time Period 3[TP-3]: 2018.08.04 to 2020.02.03

Table 3: Effect of drug over time on Platelets:

Time Period (TP)	Mean ± SD	Combination of Time Period	Absolute Mean Change of Platelets	Test Statistic Value (W)	p-value
1	0.482±0.29				
2	0.369±0.238	TP-1 vs TP-2	0.113	254.5	0.4218
3	1.267±0.878	TP-2 vs TP-3	0.898	59.0	0.0759

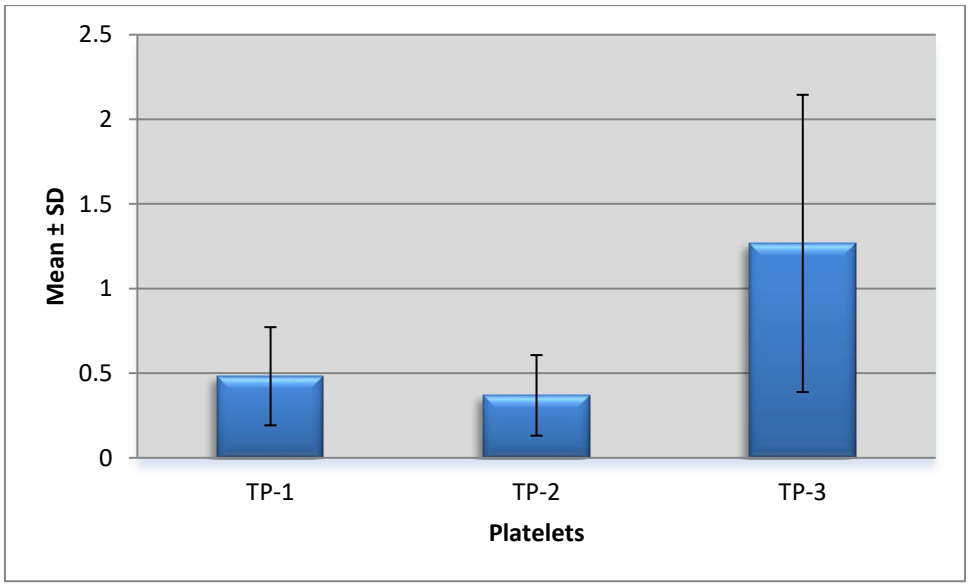

Figure-1: Improvement of Platelets over Time Period

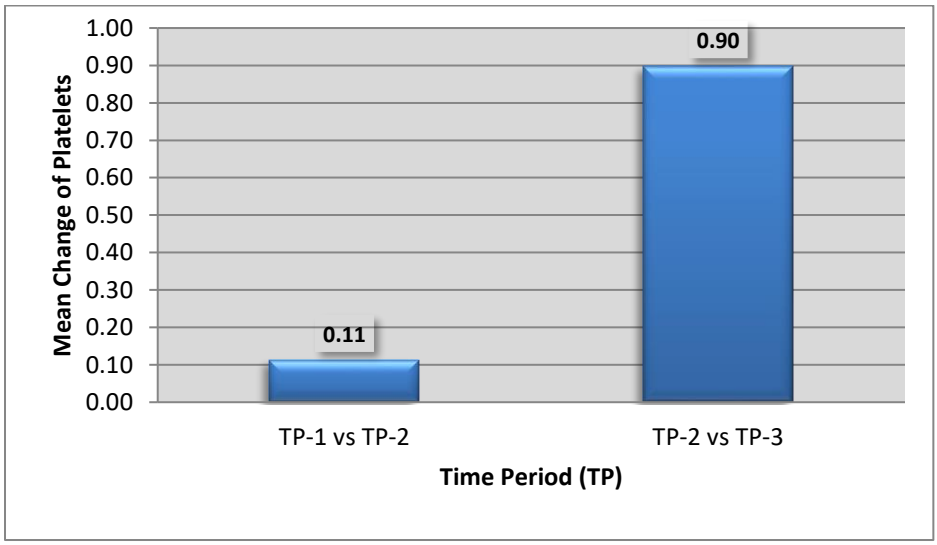

Figure- 2: Absolute Mean Change of Platelets over Time Period

OBSERVATION AND RESULT:

There was marked and meteoric improvement in blackish/bluish patches, petechial hemorrhage, buccal bullae, bleeding gums, malaena, spleenomegaly and significant peak also observed in platelet count within a first 15 days treatment.

Statistical analysis:

Improvement of Platelets over different time period was statistically analyzed using Wilcoxon-Mann-Whitney test. The result

was expressed as the Mean ± SD. P<0.05 has been considered as statistically significant and p<0.08 have been considered as marginally significant. From table 1, shows that there was no statistically significant (p-value=0.4218) improvement in between Time Period 1 and 2, but there was marginally significant (p-value=0.0759) improvement found in between Time Period 2 and 3.

DISCUSSION:

At present, for the treatment of ITP, Western medicine mainly has the following treatment measures, such as the application of glucocorticoids, platelet transfusion, gamma globulin, and the use of immune suppressants as well as splenectomy, of which about 30% of the patients have no obvious treatment effect. Some patients with ITP who have been relieved by drug treatment still have problems such as marked side effects, high price of the therapy, and easy recurrence and some patients are difficult to adhere to treatment for a long time.

The Unani pharrmacopeal formulation Sharbat **Anjbar** has styptic property and therapeutically used in hemorrhagic conditions, [11] like Nafth al-Dam (haemoptysis), Ishale Damwi (hemorrhagic diarrhea), Kathrat-i-*Hayd (*polymenorrhoea).[12]Anjbar **(**Snake Weed) has anti inflammatory, haemostatic, stringent properties and used for internal hemorrhages, irritable bowel syndrome, diverticulitis, ulcerated mouth and bleeding gums.[13] It stop bleeding and also acts as Muqawwi-i-Mi'da(Stomachic), and muqaw-i-Jiger(hepatotonic).[14],[15]

Marjan (Coral) posses haemostatic property and used in Nafth al-Dam(haemoptysis). [15] It is used in Ishale Damwi (hemorrhagic diarrhea) and acts as Muqaww*i*-i-Mi'da (Stomachic) and detoxifies liver and spleen.[16]

Zahar Mohra (serpent stone) is described as tonic for vital organ, exhilarant, antidote to poisons, protect quwa (faculties) and arwah (Vital forces), purifies and detoxifies the body humours and strengthens the muscles.[17] The pharmacological Actions of Zahar Mohra (Magnesium silicate) are Anti-phlegmatic, Anti-septic, Antidote, Astringent, Calorific, Cephalic Tonic, Cholagogue, Deobstruent, Desiccative, Refrigerant, Resolvent.[18, 20]

Majoon Dabeedulward is a Muwallid-i-dam(haemopoietic) and has mohalil-e-waram (Anti-inflammatory) action therefore used in zof-i-kabid, warm-e-kabid and Faqr al-Dam (Anaemia)[11, 19]

Gul-e-Surkh (Rose) has Habis-ud-dam (Styptic), Mohallile Waram (Anti-inflammatory), Muqawi-e-Qalb (Cardiac Tonic), Muffathe Sudad (Ant obstructive), Moqawi-e-Meda (Stomachic) Muqawi-e-Jigar (Liver Tonic) properties and used for Nafasud-Dam (Haemoptysis), Ishal (diarrhea), Sudda-e-Jigar, safrawi dast (bilious dysentery).[20-22]

Tabasheer (*Bambusabambos*) has Expectorant, Astringent, Anti-Inflammatory, Cardio tonic, Antidiarrhoeal, Digestive, Carminative, Alexiteric, Tonic, Blood-Purifier actions and used in Diarrhoea, Haemoptysis, Haematemesis, Inflammatory Conditions, Dyspepsia, Bleeding Gums, Stomatitis.[13,23]

Jawarish-e-Jalinoosacts as a tonic for vital organs and used in conditions such as Zof-e-Aza-Raeesa (Vital organs), Zof-e-Meda (Weakness of the stomach), Zof-e-Kabid (Hepatitis). [11,19]

Ravandchini (Rheum emodi) posses hemostatic, appetizer, expectorant,

astringent, tonic, purgative, stomachic and emmenagogue, diuretic, antiseptic, antitumor, chalogogue, antispasmodic, and anti-cholesterolemic and laxative immuno modulator, hepato-protective, and anti-oxidant activity. It has its uses in various disease conditions in traditional medicine such as pyrexia, hepatic disorders, jaundice, ascites, fungal infection, bacterial infection, ulcers, dysmenorrheal and constipation. It is used externally for the treatment of joint pain, Rheumatoid arthritis.[24]

Zafran (Crocus sativus) has been widely used as hepatoprotective, stimulant, antidepressant, anti- anxiety, anti-cancer, ant parkinsonism, anti-hypertensive, anti atherogenic, anti tussive, anti- diabetic, antiulcer, anti-inflammatory, anti-arrhythmic, cardio protective and as aphrodisiac agent. [25] The beneficial and protective effect of *Crocus sativus* is because of the crocin, crocetin and safranal on different enzymes of antioxidant defense system.[26]

Asaroon (*Asarum europaeu)* has deobstruent, hepotoprotective and stomachic action and used in inflammation of liver and spleen. [20]

Filfil Daraz (*Piper longum)* has desicant, deobstruent, aptetizer, expectorant actions. It is used in inflammation of spleen and improves the quality of blood. [20]

Tehali is a compound formulation of Dawakhana Tibbiya College, AMU, Aligarh which contains ingredients such as Mako khushak, revandchini, shibbe yamani, sajji safaid, tutia sabz, shora qalmi, tursha sirka, nausadar, heera kasees, latloban, maghz gheekwar etc. It is used in inflammatory conditions of spleen and blood dyscrasias.

Mako (Eclipta alba) acts as tonic, antipyretic, stomachic, anthelmintic, anti-asthmatic and expectorant. It cures inflammations, hernias, eye diseases, bronchitis, asthma, leucoderma, anaemia[27], itching, night blindness; improves the colour of the hair and promote growth. is used for jaundice, fevers, sores, skin diseases, elephantiasis and checking hemorrhages and fluxes and strengthening the gums. [28]

Alum(shibbeyamani) has haemostatic, astringent, desiccant, and antipyretic actions and used for Hemorrhagic conditions such as Bleeding gums, intestinal bleeding, epistaxis etc.[29]

Gheekwar (Aloevera) The levels of the reported glycohydrolases were elevated on treatment with Aloe vera, indicating increased turnover of the matrix. Both topical and oral treatments with Aloe vera were found to have a positive influence on the synthesis of GAGs and thereby beneficially modulate wound healing. [30]

CONCLUSION:

Based on the observations, it can be concluded that the Unani drugs are safe and effective in the management of chronic idiopathic thrombocytopenic purpura.

LIMITATION OF STUDY:

Unani Drugs have promising haemopoitic, styptic, anti-inflammatory, antioxidant and hepatoprotective activities which are already proven in various scientific studies too. However, the authors feel that a largescale study on these drugs involving larger population may be undertaken to substantiate the findings of this study.

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