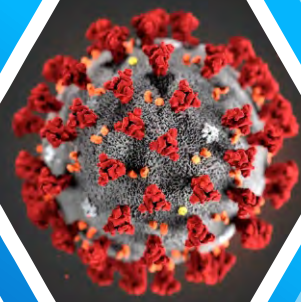


COVID-19
Coronavirus



HAEMATOLOGY UPDATES

Vol. 14, No. 1 & 2, Jan - Jun 2020

IN THIS VOLUME

- Obituary - Dr Tariq Shafi
- Pre-Conference Workshops
- HAEMCON-2020 Lahore
- Covid-19 Pandemic



PRESIDENT'S COLUMN



The current COVID-19 pandemic is creating great impact on medicine and haematology throughout the world. There is flood of information on the disease starting from epidemiology to treatment and it is difficult to filter information relevant to haematology community. Some of the important information is already being shared in our PSH group. We have included a short review on COVID-19 in the current update, PSH will also publish any information relevant to haematology in the future issues and

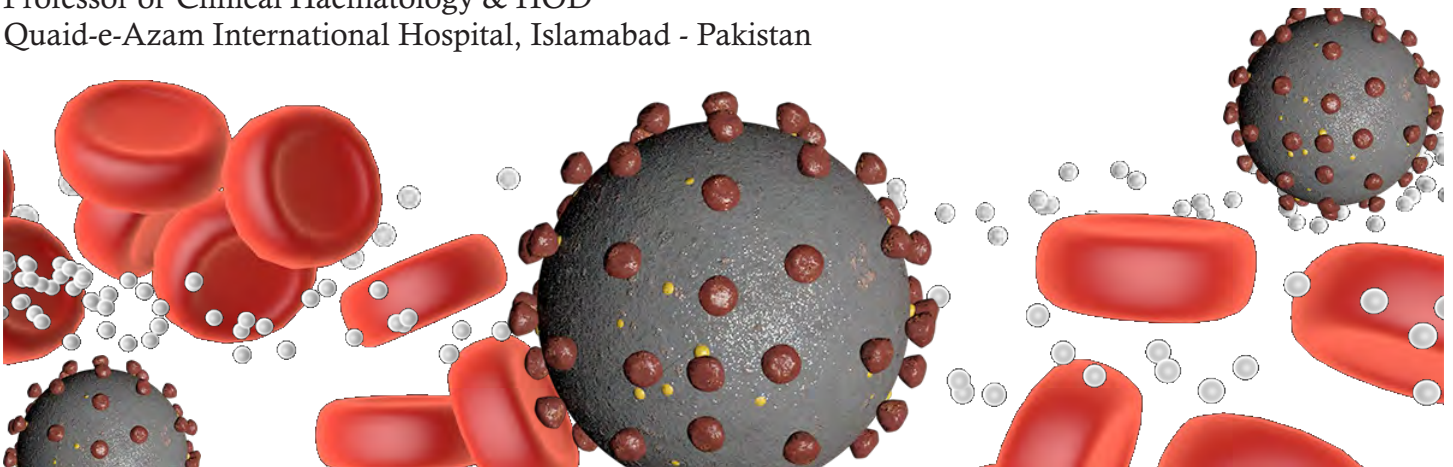
encourage the members to contribute on this major global public health problem. Due to rapidly changing scenario it remains the responsibility of each medical professional to decide on the appropriateness of medical advice, diagnosis, and treatment of COVID-19 patients. In these testing times we can help each other by active coordination and sharing of appropriate information. One of the most difficult challenges is delivering treatment to the patients with haematological disorders and to balance the risk of delaying treatment with increase mortality of corona virus infection among our patients. Closing of outpatient department and wards in some medical facilities, lack of personal protective equipment (PPE) for health care providers, limited availability of intensive care beds and movement of patients due to lockdown has compounded the complexity of management of our patients. Various measures being recommended are offering online consultations, reducing the follow up visits, delaying elective procedures, and avoiding chemotherapy and immunotherapy in conditions with marginal benefits. During these testing times we the haematology community are committed to provide best possible care to our patients.

PSH wishes all of members best of luck during these difficult times

Yours sincerely,

Dr Parvez Ahmad

President, Pakistan Society of Haematology (PSH)
Professor of Clinical Haematology & HOD
Quaid-e-Azam International Hospital, Islamabad - Pakistan



JOIN US!

Dear PSH members,

COVID19 pandemic is the biggest public health challenge around the globe.

We are blessed to have the opportunity of saving precious lives and hope we'll be able to perform our duties with honesty and sincerity during this testing time!



Community response to this pandemic seems casual and misaligned with that of medical community.

We will have to follow the changed life style during COVID19 situation. Our responsibility is to convince people for آئین نو میں:

آئین نو سے ڈرنا طرز کھن پہ اڑنا
منزل یہی کٹھن ہے قوموں کی زندگی میں

Its our responsibility to make people around us understand that washing hands, wearing masks at public places and following social distancing is definitely helpful for flattening the curve.

Replace fear with reason, panic with patience and uncertainty with faith & education!!!

Let's meet this challenge together in the best spirit of compassion for others!

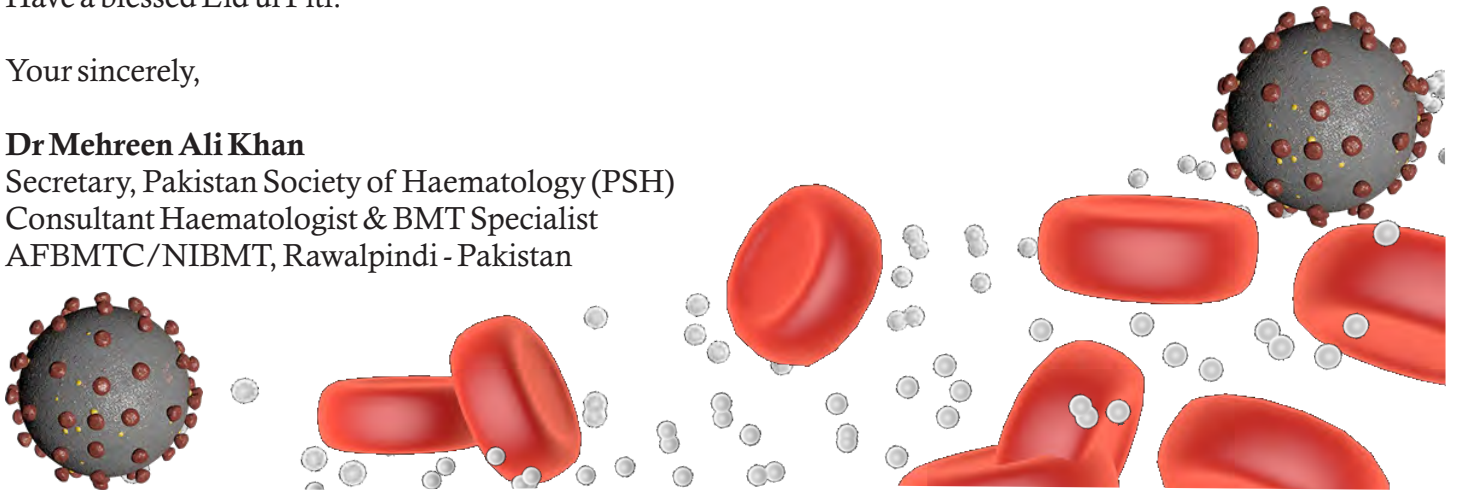
We wish all PSH members and their families safe and healthy future!

Have a blessed Eid ul Fitr.

Your sincerely,

Dr Mehreen Ali Khan

Secretary, Pakistan Society of Haematology (PSH)
Consultant Haematologist & BMT Specialist
AFBMT/C/NIBMT, Rawalpindi - Pakistan





ABOUT PSH

Pakistan Society of Haematology (PSH) was formed in 1996 with the aim of promoting advancement of haematology, BMT and transfusion medicine in the country. Presently it has more than 500 members and we all should make efforts to enroll every haematologist in the country. We request all our members to take special interest in extending the membership to all those haematologists around you who have not yet registered with PSH. Website was launched and has been very active in recent past. We are trying to rejuvenate the website "<https://www.psh.org.pk>". The website would be interactive and provide on line forum for sharing views with other haematologists, and case discussion with the experts. Other features will be facility to download online membership form, newsletter, list and addresses of the members. Hopefully the website will be more operational within this month InshaALLAH.

History:

PSH was raised as "Pakistan Society of Haematology/Transfusion Medicine (PASHT)" in 1991. A meeting was held at 5 pm on Friday Nov 22, 1991. Professor Dr Mohammad Khurshid, Brig(later Lt Gen) Muhammad Saleem, Dr Khalid Zafar Hashmi, Dr Nasim Siddiqui, and Dr Abdul Hayee attended the meeting as members in presence of Prof A. V Hoffbrand. In this meeting Dr Khurshid presented a brief outlay of the necessity to create such a society. He also pointed out that Dr. Abdul Hayee, Dr. Khurshid, Dr KZ Hashmi and Brig Saleem had met at Bahawalpur and agreed on the general principles that the first meeting would be held along with the International conference of Pathology

Though initial work was comprehensive, governing body and meetings of PASHT were not held regularly. In Sept 1994 it was proposed by Gen Muhammad Saleem to meet all PASHT members during Pakistan Association of Pathology (PAP) conference at Quetta. Dr. Muhammad Khurshid in consultation with Gen Saleem, Prof. Abdul Hayee, Dr. Khalid Zafar Hashmi proposed a provisional constitution of PASHT for the discussion in meeting.

Haematologists from all over the country met on Saturday 9 March 1996 at Hotel Pearl Continental Rawalpindi in order to form a society. It was unanimously agreed that official name of society will be "Pakistan Society of Haematology" with official abbreviation of "PSH". It was also decided that until elections for office bearers the society matters will be looked after by a committee as under

- a. Dr. Muhammad Khurshid
- b. Dr. Ehsan-ul-Allah
- c. Dr. Abdul Hayee
- d. Dr. Khalid Zafar Hashmi
- e. Dr. Khalid Hassan
- f. Dr. Masood Anwar will act as Co-ordinator

A general body meeting of PSH was held at Peshawar on 2 and 3 Nov 1996. Election for office bearers were carried out as follow



▶ ABOUT PSH

- a. Lt. Gen. Muhammad Saleem President
- b. Prof. Muhammad Khurshid as Vice President
- c. Dr. Khalid Hassan as Secretary/treasurer

Later in Oct 1997 appointment of vice president was renamed as president elect.

List of past presidents includes

1. Prof. Dr. Abdul Hayee
2. Prof. Dr. Abdul Khaliq
3. Prof. Dr. Muhammad Khurshid
4. Prof. Dr. Khalid Zafar Hashmi
5. Maj. Gen. Masood Anwer
6. Prof. Dr. Khalid Hassan
7. Maj. Gen. Suhaib Ahmed
8. Prof. Dr. Samina Naeem
9. Maj. Gen. Muhammad Ayyub
10. Prof. Dr. Nisar Ahmed

List of past secretaries includes

1. Dr. Khalid Hassan
2. Col. Massod Anwar
3. Prof. Fazle-e-Raziq
4. Dr. Salman Naseem Adil
5. Dr. Shaheena Kauser
6. Brig. Nadir Ali
7. Brig Pervez Ahmed
8. Dr. Nadeem Ikram
9. Dr. Humera Rafiq
10. Brig. Tariq Mehmood Satti
11. Dr. Saima Farhan

PSH was registered with Govt of Pakistan on 8 August 1998(RS/ICT/298 dated 8 Aug 1998 as non political and non sectarian body to promote advancement of haematology including transfusion medicine through encouragement of research, teaching and technical methods. The body will also organize scientific meetings, publication of scientific material, and affiliation with other National and international organizations. Members of Governing body included

- a. Lt. Gen. Muhammad Saleem as President
- b. Dr. Khalid Hassan as General secretary
- c. Dr. Birgees Mazhar Qazi as member
- d. Dr. Waseem Iqbal as member
- e. Dr. Hassan Abbas Zaheer as member
- f. Dr. Mobina Ahsan Dhodhy as member
- g. Dr. Farah Yasin as member
- h. Col. Masood Anwar as member

It was also decided that first National conference will be held on 4 Oct 1998. Since then Annual conference is held regularly in all capital cities of Pakistan. The society is publishing a quarterly newsletter and providing a forum to the haematologists all over the country contributing as advisors in haematology, consultants, researchers and mentorship. Currently the Governing body includes

Prof. Dr. Parvez Ahmed as President
Prof. Dr. Salman Naseem Adil as President Elect
Dr. Mehreen Ali Khan as Secretary/Treasurer



ABOUT PSH ◀

New Executive Committee was elected during 21st Annual Conference of Pakistan Society of Haematology (PSH) held at Karachi from 14th - 16th March 2019. Following are the office bearers of Executive Committee:



Dr. Parvez Ahmed
President
Cell: +92 300 8561288
Email: parvez101@yahoo.com



Dr. Salman Naseem Adil
President Elect
Cell: +92 300 9249027
Email: salman.adil@aku.edu



Dr. Mehreen Ali Khan
Secretary/Treasurer
Cell: +92 333 5164941
Email: mehreen35@hotmail.com

EXECUTIVE MEMBER COUNSEL:

Armed Forces

Qamar Un Nisa Chaudhry
Asad Mahmood Abbasi
Muhammad Sajid Yazdani

Islamabad

Nadeem Ikram

Punjab

Saima Farhan
Muniza Junaid
Muhammad Irfan Khan

Sindh

Syed Muhammad Irfan
Ikram Din Ujjan
Muhammad Nadeem

Baluchistan

Hayat Ullah

Khyberpakhtunkhwa

Shahtaj Masood

Azad Kashmir

Zahida Qasim

Office Coordinator / IT Manager

Imran Waheed
Tel: +92 51 9270076 Ext. 228 Mob: +92 322 5181302
Email: psh.org.pk@gmail.com



ABOUT PSH

RAWALPINDI/ISLAMABAD

Dr Asad Mehmood Abbasi
asadabbasi739@yahoo.com
03215506566

KARACHI

Dr Bushra Moiz
bushra.moiz@aku.edu
0300-2160765

LAHORE

Dr Muneeza Junaid
dr.mjunaaid10@gmail.com
0333-8029026

QUETTA

Dr Hayat Ullah
hayatdotani@yahoo.com
03337520574

PESHAWAR

Dr Shahtaj Masood
shahtajmasood@yahoo.com
0333-9118335

AZAD KASHMIR

Dr. Zahida Qasim
dr_qasim2011@hotmail.com
0333-5875122

SCHEDULE OF MONTHLY MEETING:

RAWALPINDI / ISLAMABAD

Date:	Last Thursday of the Month
Time:	03:00pm to 05:00pm
Coordinator:	Dr Asad Mahmood Abbasi
Venue:	AFIP, Rawalpindi

KARACHI

Date:	Last Friday of the Month
Time:	08:00am to 09:00am
Coordinator:	Dr Bushra Moiz
Venue:	AKUH, Karachi

LAHORE

Date:	2nd Tuesday of the Month
Time:	09:00am to 10:00am
Coordinator:	Dr Muneeza Junaid
Venue:	CIP, Lahore

QUETTA

Date:	Last Friday of the Month
Time:	09:00am to 10:00am
Coordinator:	Dr Hayat Ullah
Venue:	RMC, Quetta

PESHAWAR

Date:	3rd Thursday of the Month
Time:	12:00pm to 01:00pm
Coordinator:	Dr Shahtaj Masood
Venue:	HMC, Peshawar



DR. TARIQ SHAFI (1958-2020)

BSc, MBBS, FRCP (Lon & Edin), FRCPath (UK)

By Maj Gen (Retd) Parvez Ahmed, HI(M)

OBITUARY

On 6th May 2020 Haematology community and PSH lost a brilliant and noble professional Dr Tariq Shafi to COVID-19 while working on the frontline fighting the deadly corona virus in UK. He developed symptoms of COVID-19 on 2nd April 2020 but continued to work for his patients from home until his admission. On 9th April he was admitted to Darent Valley Hospital Dartford, Kent UK, the same hospital where he worked as consultant haematologist for 13 years; and shifted to ICU on 12th April 2020. His health unfortunately deteriorated and he was put on ventilator, was subsequently shifted to St Thomas Hospital in Central London on 24th April. On the afternoon of 6th May, Dr Shafi passed away despite the best efforts of some of the best doctors to save him. Tariq passed away in the blessed month of Ramzan in the line of duty. "Verily we belong to Allah, and verily to Him do we return."

Dr Tariq Shafi was 61, a humble and dedicated person and one of the finest doctor, who cared deeply for his patients and colleagues. Born in Lahore Pakistan to Brigadier Muhammad Shafi and Mrs. Mumtaz Durrani Shafi in 1958. He attended Cadet College Hassan Abdal leaving it in 1976, graduated from King Edward Medical College Lahore in 1984. He moved to UK in 1988, completed general medical training and did MRCP in 1991 and joined Haematology training as registrar. He moved to Saudi Arabia in 1994 where he worked in Military Hospital Riyadh till 2007, completed MRCPPath in 1997. He also underwent specialist training as bone marrow transplant coordinator in King's College Hospital London from 2000-2001. He remained Consultant Haematologist and Bone Marrow Transplant Physician, in Riyadh, Saudi Arabia. Moved to UK in 2007 and took up the post as Consultant Haematologist and Head of Department at Darent Valley Hospital UK. He never lost touch with Pakistan and helped Pakistani doctors to come to the UK for further training.

I don't remember the exact year; probably it was 2012, when I met Dr Tariq Shafi; with his signature warm smile on the face and a pleasant personality, in one of the Annual PSH conferences. He was eager to contribute



OBITUARY



for the progress of haematology in Pakistan. We discussed few options like holding regular workshops and encouraging our young haematologist to find training slots in UK. He mentioned about his acquaintance with famous UK haematologist, Prof Ghulam Jeelani Mufti at King's College Hospital London and suggested me to talk to him and invite him at Armed Forces Bone Marrow Transplant Centre Rawalpindi. Throughout this time we have been in touch with each other. We were able to arrange training of four young haematologists from Pakistan Army at King's College Hospital London and invited Prof Mufti for scientific talk at our centre on 14 Nov 2016. He was a regular contributor in Annual PSH conference and conducted workshops whenever requested. During Haemcon 2020, he was keen to invite Prof Ghulam Jeelani Mufti, who always has extremely busy schedule but through Tariq's persistent efforts we were able to get Prof Mufti in the Haemcon 2020 and a short visit to AFBMTC Rawalpindi. His latest contribution is arranging paid slot for Dr Hayat Ullah Dotani, our brilliant young clinical haematologist from Quetta at Darent Valley Hospital UK. His contributions towards the development of haematology in Pakistan would be remembered in golden words.

Whole of the Haematology Community in Pakistan is in shock and feel devastated on the sad demise of this extremely loving and caring friend and pray to Allah The Almighty to shower His countless bounties and rahmah upon this noble soul and rest him in eternal peace and tranquility. Ameen. We, The Pakistan Society of Haematology extend our sincerest and heartfelt condolences to the grieved family of Dr Tariq Shafi and pray to Allah to give them strength and courage to bear his loss.



PRE-CONFERENCE WORKSHOPS

Haemcon 2020 10th Pre Congress workshop on **Quality Assurance in Haematology** was held in General Hospital, Lahore on 9th January 2020. It was attended by a large number of consultant Hematologists and Post Graduate residents. Program started by recitation of Holy Quran followed by welcome address given by Assoc Prof Haematology. PGMI/AMC/LGH Dr Nighat Rashid. Prof Dr. Nisar Ahmed chief coordinator Haemcon2020 was guest of honor.

Chief Guest of the Symposium was Dr. Muhammad Al Farid Zafar, principal Post Graduate Medical Institute/Ameer ud din Medical College/Lahore General Hospital, Lahore. He addressed the audience and thanked respected speakers to make this workshop successful by sharing their knowledge and expertise.

Participants were given pre workshop assessment proforma. First lecture was delivered by Prof. Brig (R) Dr. Aamir Ijaz on introduction to Quality assurance. This was followed by a series of talk on Quality Assurance by Prof. Brig (R) Dr. Nuzhat Mushahid which included selection of method/assay, verification/validation of laboratory analytical methods and reagents, test performance assessment and external quality assurance. She highlighted important aspects and introduced new key points for implementation of quality assurance in laboratory practices. Dr Humera Rafique Assoc Prof Haematology, PGMI/AMC/LGH gave a comprehensive presentation on validation of instruments.

The souvenirs and shields were presented to Speakers and organizing committee. The symposium was concluded by vote of thanks.



PRE-CONFERENCE WORKSHOPS

A pre conference symposium on **Approach towards bleeding disorders** was held on January 18th, 2020 in CMH Institute of Medical Sciences in the beautiful city of Bahawalpur.

This workshop included talks from noteworthy speakers from the field of Haematology ie Maj. Gen. Parvez Ahmed, Prof Nisar Ahmad, Brig. Ch Altaf Hussain, Dr. Saima Farhan, Lt. Col. Raheel Iftikhar, Dr. Mohammad Irfan Khan and Maj. Shaan e Rauf.

The workshop arrangements were effectively done by Dr. Javeria Fatima of Children Hospital Lahore and this symposium provided an excellent overview of the bleeding disorders with an effective interactive session in the end. Brig. Ch Altaf Hussain, Principal of the CMH Institute of Medical Sciences Bahawalpur proved to be an excellent host and made all the team visit the important sites of city next day with an extravagant dinner and historical light show at the beautiful Noor Mehal of Bahawalpur. It was a memorable experience.



PRE-CONFERENCE WORKSHOPS

Haemcon 2020 A hands on pre-conference workshop on **Haemato-oncology** at Shifa International Hospital, Islamabad on 25th January 2020. Twenty teaching cases of Haematooncology were discussed by four Haematology Consultants from Shifa International Hospital, Islamabad. Participants from Rawalpindi/Islamabad and Peshawar were registered and contributed actively.



Armed Forces Bone Marrow Transplant Centre / National Institute of Blood & Marrow Transplant (AFBMTC/NIBMT) Rawalpindi organized a hands on pre-conference workshop on **Bone Marrow Transplant Nursing** on 25th January, 2020. It was attended by a large number of participants from difference institutes and hospitals. Program started by recitation of Holy Quran followed by welcome address given by Brig. Qamar Un Nisa Chaudhry, Commandant AFBMTC/NIBMT, Rawalpindi. Maj Gen Parvez Ahmed, HI(M) (Retd), President PSH was guest of honor.



PRE-CONFERENCE WORKSHOPS

A workshop on **Pediatric Bone Marrow Pathology** was conducted in AIMC/Jinnah hospital on 01 Feb 2020 organizers and lecturers included Dr Fauzia Shafi Khan pediatric hematologist CH/ICH and Dr Asad Hayat Consultant hematologist SKMH. Dr Sami PGR Haematology from CH/ICH coordinated the whole event flawlessly. It was the first ever hands-on workshop dedicated solely to both pediatric benign and malignant bone marrow disorders.

Cases selected included rare potentially misleading presentations of some common disorders in addition to a wide range of pathologies from some common to very rare ones which one would not see in an adult setup. The emphasis was on an integrated approach to diagnosis utilizing clinical information, peripheral smear, marrow aspirate, trephine & IHC findings.

The event was very well attended with some participants travelling from far away for it. The workshop got some excellent feedback with requests for continuation of similar activities to continue in future.



PRE-CONFERENCE WORKSHOPS

Pre-conference workshop on thrombosis was held at Services Institute of Medical Sciences (SIMS), Lahore on 10th February, 2020 in collaboration with Pakistan Society of Haematology. It was convened by Prof Faiza Bashir (Professor of Haematology) and facilitated by Dr Asma Munir and the haematology section, Pathology Dept, SIMS.

Proceedings began with Prof Faiza Bashir's welcome address for the honorable speakers and guests. It was followed by address by Prof Nisar Ahmad, guest of honour for the occasion. He announced that it was the first workshop on thrombosis being held at the PSH forum and an excellent opportunity for the participants to update themselves. Chief guest of the workshop was Principal SIMS/SHL & PIMH Prof Mahmood Ayyaz. In his address he expressed pleasure that department of Pathology had brought together both national and international experts to share their knowledge.

In first session Dr Tariq Shafi, consultant haematologist working at Darent Valley Hospital, UK elaborated the association of Cancer with thrombosis. The next presentation was by Dr Usman Ahmad Consultant Clinical Haematologist at SKMCH&RC, Lahore. The audience actively gave their input as he discussed clinical details of cases that developed thrombosis due to acquired causes.

In second session Dr Tariq Shafi highlighted both basic and advanced concepts of anticoagulation. The workshop ended with a detailed question and answer session. Prof Faiza Bashir concluded the session and Prof Mahmood Ayyaz distributed shields& souvenirs to the speakers and organizers of the workshop.



► PRE-CONFERENCE WORKSHOPS

Pakistan Kidney and Liver Institute and Research Centre was privileged to conduct a one day hands-on workshop on **Blood Banking skills and methods**, organized by the Department of Haematology and Pathology on 11th February, 2020.

The main features of the event included lectures encompassing various aspects of blood transfusion services, which were delivered by Consultant Haematologist and Blood Bank Director, Dr. Unaiza Qamar, Consultant Immunologist Dr. Nida Saleem, and Senior Registrar Haematology, Dr. Anum Wasim, and a meticulously planned hands-on workshop for the candidates, thanks to the tireless efforts of the Blood Bank staff. They were given the opportunity to test their practical skills on blood grouping, cross match and antibody screening methods.

The occasion was graced by the presence of Dean PKLI, Prof. Dr. Hafiz Ejaz Ahmed, Professor of Haematology, Prof. Dr. Nisar Ahmed, and PKLI Lab Director, Brig. (R) Dr. Muhammad Atique. The participants showed a keen interest during the interactive lectures, and were pleased with the invaluable experience gained at the well-equipped PKLI Blood Bank. The PKLI Pathology Dept. hopes to conduct more of such workshops and seminars in the near future, contributing to the development of skilled Pathologists in Pakistan.



**22nd PSH Annual Meeting & Conference**February 13-16, 2020
Avari Hotel, Lahore - Pakistan**HAEMCON-2020 LAHORE**

The Children's Hospital and Institute of Child Health Lahore had the honor and pride of organizing the Haemcon 2020 22nd PSH Annual International Congress from 13th to 16th February at the Avari Hotel Lahore. Prolific haematologists from Pakistan & abroad took part in the event.

Professor Dr. Yasmin Rashid, Minister Primary and Secondary Specialized Healthcare and Medical Education Government of Punjab was chief guest.

Respected and honorable professor Abdul Hayee, Professor Yasmin Lodhi, VP LMDC, Professor Khalid Masood Gondal, VC KE University and Professor Masood Sadiq, Dean of Children Hospital Lahore were the guest of honor at the opening ceremony. The event was, ably hosted Dr. Javaria Fatima & Dr. Sara Rafi started with recitation and the national anthem. Dua & tribute was given to General M Saleem (late) by General Sohaib Ahmad. This was followed by the welcome address of the chairperson Dr. Saima Farhan, Associate Professor Paediatric Haematology, the Children Hospital Lahore and a speech by President PSH Major General Parvez Ahmed, HI(M).

State of the art lecture "Overview of Bone Marrow Failure" was delivered by Professor Dr. Ghulam J. Mufti from King's College Hospital London, UK. Whereas Professor M Khurshid from Aga Khan University Hospital, Karachi presented Ibn e Sina lecture on "Haemovigilance in Transfusion"

Secretary Organizing Committee Assistant Professor Dr. Shazia Yaseen, Children Hospital Lahore thanks the attendees & formal inauguration of scientific exhibition took place followed by a high tea.

Registration for Congress was started months in advance and continued till the final day of the Congress. Over 600 participants were issued registration cards, lunch, gala dinner token and souvenir bag with key-rings, dairies, required literature etc. The entire process was well organized.

Many pharmaceutical companies put up their beautiful stalls displaying latest electro-medical equipment and literature regarding various drugs which are used in patients suffering from haematological diseases. It too was organized very well.



HAEMCON-2020 LAHORE

INAUGURAL
February 13, 2020





DAY-1

February 13, 2020

HAEMCON-2020 LAHORE





HAEMCON-2020 LAHORE

DAY-1
February 13, 2020





DAY-2
February 14, 2020

HAEMCON-2020 LAHORE





HAEMCON-2020 LAHORE

DAY-2
February 14, 2020





DAY-3

February 15, 2020

HAEMCON-2020 LAHORE





HAEMCON-2020 LAHORE

DAY-3
February 15, 2020





GALA DINNER February 14, 2020

HAEMCON-2020 LAHORE





COVID-19 PANDEMIC

Hematological Aspects of Covid-19

Dr Raheel Iftikhar

MBBS, FCPS (Medicine), FCPS (Clinical Haem), FACP (USA), MAAFP (USA)

Introduction:

First reported from Wuhan China in late December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) causes coronavirus disease 2019 (COVID-19) and has currently spread to 212 countries affecting more than 4.2 million people worldwide. SARS-CoV2 bears many resemblances with SARS-CoV and invades host cells by binding to angiotensin converting enzyme 2 (ACE2) receptor(1). Initially reported to present as pneumonia, it is now recognized that COVID-19 is a systemic disease with multisystem manifestations involving pulmonary, cardiovascular, neurological, gastrointestinal, immune and hematopoietic systems(2, 3). Hematologist role in management of current pandemic is to deal with patients of pre-existing hematological disorders who acquire COVID-19 and management of patients developing hematological complications. Recent data suggest 30 days mortality rates of up to 40% among patients of pre-existing hematological disorders acquiring COVID-19 infection(4). Hematological and immune abnormalities are seen more frequently in patients with severe disease and used as markers of monitoring disease progression(5). Management challenges include early recognition and treatment of dissemination intravascular coagulation, rationale use of anti-coagulants, blood component support and selection of patients to receive trial therapies like convalescent plasma(6), plasma exchange(7) and tocilizumab(8). Moreover, considering very high mortality rates of COVID-19 among patients with pre-existing hematological disorders, there is need to prioritize administration of chemotherapy and hematopoietic stem cell transplant (HSCT) procedures based on co-morbidities, underlying disease status, medical resources and available supportive care facilities to reduce treatment related morbidity and mortality.

Epidemiology and Pathogenesis of Covid-19:

There has been exponential increase in the number of cases worldwide since first reported case in late December 2019. More than 5 million confirmed cases in 212 countries have been reported. Mortality rate is lower (3.8%) as compared to SARS-CoV2 10% and MERS-CoV (37.1%) but transmission rates are 10 times higher(9). Older age, pre-existing co-morbidities (diabetes mellitus, hypertension, ischemic heart disease) are risk factors for severe COVID-19 (10). Data from China and France have documented higher incidence of adverse events in patients with pre-existing solid organ (11) and hematological malignancies (4). Most of coronaviruses are known to infect humans and various animals(9). Although origin of SARS-CoV2 outbreak has not yet been identified, transmission caused by bats, snakes and pangolins has been reported(12). Person to person transmission mainly occurs by respiratory droplets, direct contact with infected surface and touching eyes, nose or mouth. Analysis of viral genome has revealed that SARS-CoV2 is phylogenetically close to SARS-CoV previously reported in 2002 (13). SARS-CoV2 primarily affects tissues expressing high levels of ACE2 receptors including the lungs, heart and gastrointestinal tract(3). Lymphocytes also express ACE2 receptors on their surfaces with resultant lymphopenia occurring in around 80% of symptomatic patients and correlate with disease severity(14). SARS-CoV-2 may impair the function of CD4+ helper and regulatory T-cells and promote the initial hyperactivation which is followed by rapid exhaustion of cytotoxic CD8+ T-cells(15) leading to hyperinflammatory and cytokine release syndrome(CRS). It is characterized by markedly increased interleukin (IL)-2, IL-7, granulocyte-colony stimulating factor, interferon- inducible protein 10,

COVID-19 PANDEMIC

monocyte chemoattractant protein 1, macrophage inflammatory protein 1- α , and tumor necrosis factor- α promoting atrophy of lymphoid organs leading to lymphocyte apoptosis(16). Thrombocytopenia is frequently encountered and possible mechanism of thrombocytopenia in COVID-19 include immune mediated destruction, cytokine storm, increased consumption due to lung injury and direct toxic effect on bone marrow megakaryocytes(17). COVID-19 associated coagulopathy (CAC) can lead to widespread thrombosis or bleeding manifestations. Elevations of d-dimers and fibrinogen levels are most common pattern of coagulopathy and correlates with increase in markers of inflammation. In contrast to classic DIC resulting from bacterial sepsis or trauma, aPTT elevation is often less than PT elevation, degree of thrombocytopenia is mild and microangiopathy is absent in patients with CAC. Patients with hematological malignancies are more prone to severe COVID-19 and have coexisting lactic acidosis and more severe lymphopenia (18). Venous thromboembolism and arterial thrombosis is increasingly reported in COVID-19 patients. The possible mechanisms include endothelial cell damage and activation due to the virus binding to ACE2 receptor and release of inflammatory cytokines leading to prothrombotic state. Moreover, immobilization, mechanical ventilation, central venous catheterization may predispose to prothrombotic state.

Clinical Manifestations:

Spectrum of clinical presentation ranges from asymptomatic to critical disease requiring mechanical ventilation. Most common symptoms include fever, dry cough, fatigue and shortness of breath. Initially COVID-19 pneumonia was considered to be the cause of death but now there is evidence from literature around the globe that severe COVID-19 presents as multisystem disease involving neurological, pulmonary, cardiac, gastrointestinal, renal and hematopoietic system. Confusions, diarrhea, thrombosis, arrhythmias, myocardial infarction are among less common manifestation. Very little data is available on outcome of patients with hematological disorders acquiring SARS-CoV2 infection. Malard *et al* reported fever, cough, shortness of breath and lymphopenia as most common clinical presentations among patients with pre-existing hematological diseases having COVID-19. Among affected patients, 52% developed ARDS and mortality at 1 month was 40%, which is significantly higher than other risk groups. Importantly less than half patients were receiving active treatment, indicating immunocompromised status due to previously administered chemotherapy contributed towards poor survival outcomes(4).

Haematological and Biochemical Abnormalities:

A wide variety of haematological manifestation are seen among patients with Covid-19. These range from normal values to leukocytosis, lymphocytopenia, monocytopenia, thrombocytopenia and coagulation defects (3, 19, 20). Antiphospholipid antibodies and widespread thrombosis causes ischemic stroke, myocardial infarctions, venous thromboembolism have been documented in COVID-19(21). Increased tissue penetration of SARS-CoV2 results in release of inflammatory cytokines leading to secondary hemophagocytic lymphohistiocytosis (sHLH) and cytokine storm. Affected patients develop high grade fever, cytopenias, visceromegaly, hypofibrinogenemia, coagulopathy progressing to multiorgan dysfunction syndrome and poor prognosis.



COVID-19 PANDEMIC

Prognostic Significance of Haematological Abnormalities:

Different studies have documented prognostic significance of laboratory abnormalities in SARS-CoV2 pandemic. Hematological abnormalities commonly reported are leukopenia (25-37%), lymphopenia (36-83%), thrombocytopenia (5-36%), (19, 20). Neutrophil lymphocyte ratio has prognostic value in determining disease severity. Monitoring lymphocyte count dynamics and inflammatory markers (CRP, ferritin, IL-6, LDH) may help to identify cases with worse prognosis and need for prompt intervention to improve outcome. Elevated d-dimers are reported in patients with moderate to severe disease and their rise during disease course is indicator of worsening of disease (5, 19). Moreover, hyperferritinemia, prolongation of PT, aPTT, hypofibrinogenemia, thrombocytopenia are markers of severity, progression to critical disease and poor prognosis. Studies have shown that patients admitted to ICU had more marked leukocytosis, lymphopenia, prolonged prothrombin time and d-dimers as compared to non-ICU patients (3, 20), 96.1% versus 80.4% for lymphocytopenia, 57.7% versus 31.6% for thrombocytopenia and 61.1% versus 28.1% for leukopenia. Huang et al. found an association between lymphopenia and need of ICU care (20), whereas Wu et al. showed higher incidence of acute respiratory distress syndrome (ARDS) development in patients with lymphopenia (22). Comparison of patients with severe disease demonstrated a decreased lymphocyte/white blood cell ratio both at admission ($p < 0.001$) and during hospitalization ($p < 0.001$) compared with those who survived (15). Patients with cardiac dysfunction had higher white cell count ($p < 0.001$), lower lymphocyte ($p < 0.001$) and platelet counts ($p < 0.001$) (23). Wu et al. reported that higher serum ferritin was associated with ARDS development and poor outcome (22). Coagulation disorders are frequently encountered among COVID-19 patients, especially among those with severe disease (24). D-dimer elevation and DIC are common in patients with severe COVID-19 infection and the scoring system for compensated and overt DIC endorsed by the International Society on Thrombosis and Hemostasis should be followed for early DIC identification. Based on the recently published data, we propose longitudinal monitoring of WBC, lymphocyte count, D-dimers, ferritin, prothrombin time and platelet count in all patients who present with COVID-19 infection. This may help in predicting patients at risk of severe disease, in order to plan early intervention and critical care support.

Management:

Management of patients with COVID-19 involves multidisciplinary team approach with aim of risk stratifying patients as per severity and to provide optimal supportive care and timely intervention. Hematologist opinion is frequently sought for cytopenias, rise in inflammatory markers and coagulopathy. Moreover, management of patients with pre-existing hematological disorders and HSCT recipients are at increased risk of severe COVID-19 and careful selection and monitoring is required for such cases.

Coagulopathy:

1. All patients with COVID-19 should undergo platelet count, d-dimers, fibrinogen, prothrombin time testing at initial diagnosis and then serially. Ideal interval for serial monitoring is not defined.
2. All patients with COVID-19 should receive prophylactic anticoagulation unless contraindicated. Low molecular weight heparin (LMWH) is preferred (26).

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3. Therapeutic anticoagulation should be considered for high-risk coagulopathy (including CRRT and ECMO), documented thromboembolism and signs of microthrombi induced organ dysfunction(25).
4. Aspirin should be considered in patients with elevated troponin and cardiac dysfunction.
5. Thresholds for transfusion of blood products are as follows
 - a. No active bleeding: Keep platelet count $>25 \times 10^9/L$
 - b. Active bleeding: Keep platelet count $>50 \times 10^9/L$, plasma fibrinogen $> 1.5 \text{ g/L}$, PT ratio <1.5 .

Management of coagulopathy in COVID-19 is summarized in figure 1:

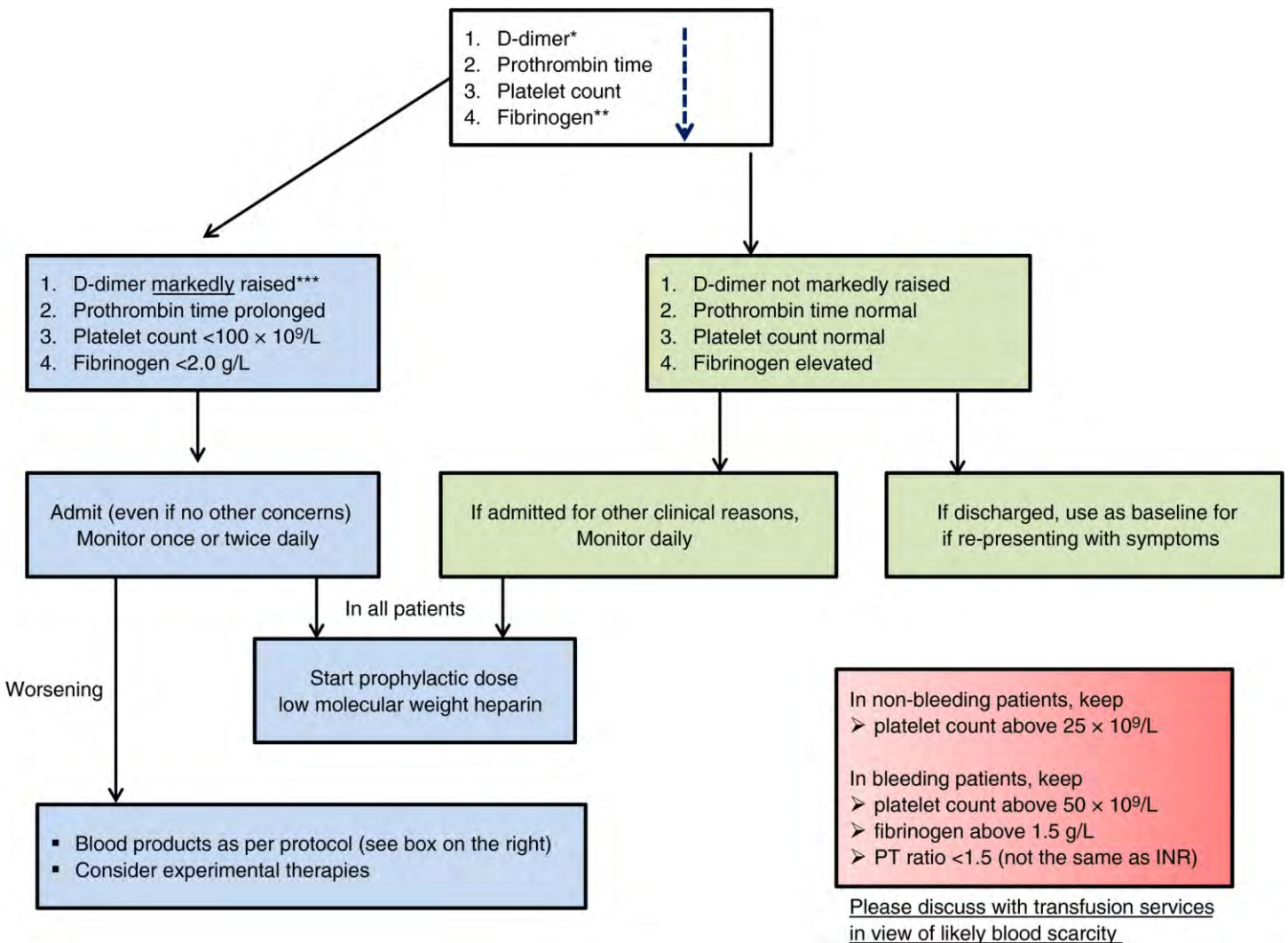


Figure 1: Algorithm for the management of coagulopathy in COVID-19 based on simple laboratory markers. * The list of markers is given in decreasing order of importance. ** Performing fibrinogen assays may not be feasible in many laboratories but monitoring the levels can be helpful after patient admission. *** Although a specific cut-off cannot be defined, a three- to four-fold increase in D-dimer values may be considered significant. Any one of the values in this table may be considered significant



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Trial Drugs:

Convalescent plasma: An initial pilot study from China documented feasibility of CP in COVID-19 and suggested potential benefit(27). Another study by Chen C et al explored potential role of CP in reducing Cytokine Storm (28). A Systematic review on Potential interventions for COVID-19 suggested use of CP to reduce mortality and hospital stay(29). A recent case series of 5 critically ill patients of COVID-19 and ARDS treated with CP documented clinical improvement in all 5 patients(30). On March 24, 2020 FDA authorized use of CP for investigational use under the traditional IND regulatory pathway (21 CFR 312). As a principle, passive immunization is more effective for prophylaxis and when given early in disease course due to low disease burden being neutralized by antibodies in CP. It is important to emphasize that use of CP in COVID-19 is still experimental and it is important to conduct a randomized trial to assess efficacy of CP in COVID-19. Currently different trials are exploring its role in post exposure prophylaxis, moderate COVID-19 and patients with critical illness caused by SARS-CoV2.

Mesenchymal stem cells(31): Initial study from China (Zikuan Leng et al published in Journal of Aging and diseases, February 2020) enrolled 10 patients suffering from severe COVID-19 pneumonia (7 study arm, 3 controls) used single dose of third party Clinical grade MSCs at dose of 1 million cells/kg body weight. Subjects continued to receive all other supportive and therapeutic treatments concomitantly. All patients in Study arm survived as compared to 2 out of 3 patients in the control arm with one of the two survivors having severe Acute Respiratory distress syndrome at time of study publication. Currently 10 studies are registered with Clinicaltrials.gov for use of Mesenchymal Stem Cells in COVID-19, eight are from Wuhan China, 1 from Brazil and 1 from Saudi Arabia, Jordan and four of the studies are actively recruiting subjects. Existing data shows that possible beneficial effect of MSC can be attributable to immunomodulatory properties(31).

Plasmapheresis: Recent literature has documented possible beneficial role of plasmapheresis in COVID-19 patients. Possible role include removing inflammatory cytokines, stabilizing endothelial membranes, and resetting the hypercoagulable state(7).

Management of patients with pre-existing hematological diseases:

Patients with hematological malignancies are very vulnerable to COVID-19 infection. A recent French study showed 40% mortality at 1 year and patients of multiple myeloma being at high risk of severe illness with COVID-19(4). It is therefore important that hematology departments should remain COVID-19 free zones dedicated strictly to hematological treatments(4). Hematologists should prioritize chemotherapies for patients with hematological malignancies in order to reduce SARS-CoV2 risks for patients and health care providers without compromising effective management. Some of the steps recommended by EHA and EBMT are as follows

1. Switch to oral drugs
2. Avoid calling patients for routine clinic visits
3. Administer drugs at home, wherever possible

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4. Switch to once weekly administrations of drugs to reduce hospital visits
5. Change outpatient clinics to telemedicine

EHA and EBMT recommendations for treatment of hematological diseases during COVID-19 pandemic are summarized in table 1

Hematologic Disease	Recommendation
Aggressive lymphomas	Initial therapy: no change, outpatient visits as much as possible Visits: replaced with telemedicine Rescue therapy: delivered in the outpatient setting if possible Auto-SCT: defer
Indolent lymphomas	Asymptomatic: watch-and-wait approach (instead of rituximab, for example) Chemotherapy: defer as much as possible; use R-COP/R-CHOP regimens in place of bendamustine Maintenance: defer onset of rituximab, e.g. in patients with FL, and increase the intervals between rituximab cycles. Use ibrutinib for MCL and CLL
Hodgkin lymphoma	Localized stages: avoid radiotherapy (multiple sessions) Advanced stages: Use ABVD regimens or similar, telemedicine, and outpatient regimens with bendamustine for relapse. Defer auto-SCT and allo-SCT
AML	Before therapy: conduct a PCR test (mandatory) Induction: use standard regimens and extreme prophylactic measures Consolidation: aim to use home protocols Allo-SCT: do not excessively delay Relapsed patients: enroll in clinical trials if possible
Multiple myeloma	MM without CRAB symptoms: delay onset of treatment Induction and maintenance therapy: do not change for both transplant eligible and ineligible patients COVID-19 infection: interrupt maintenance until infection resolved Clinic visits: decrease as much as possible using remote labs, telemedicine, and prescription delivery via mail SCT: delay until the pandemic abates
Aplastic anemia	Immunosuppressive therapy: Avoid use of T-cell depleting therapies except those with severe cytopenias with immediate risk of death due to severe neutropenia or major bleeding. Thrombopoietin agonists are preferred for most of patients and can be used as bridge to more intensive therapy. Allogeneic HSCT: Wherever possible, postpone transplant. In case of very severe disease with life threatening features, proceed to HSCT following COVID -19 guidelines for donor and recipient

Table 1: EBMT and EHA recommendations for treatment of hematological malignancies during COVID-19

Blood Transfusion:

Currently there is no evidence to suggest transmission of SARS-CoV2 through transfusion of blood products(33).

Conclusion:

Hematological manifestations of COVID-19 and SARS-CoV2 infection among hematology patients has been frequently reported in recent literature. Careful monitoring of hematological parameters at outset and during

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disease course are useful to identify patients at high risk of severe disease. Timely initiation of thromboprophylaxis, identification of DIC and use of trial drugs can help to reduce adverse outcomes in critically ill patients. Hematologist should prioritize use of chemotherapy among patients with hematological malignancies to reduce risk of life threatening COVID-19 among patients and exposure to health care workers.

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(References truncated, complete list can be found in the article published elsewhere)



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The PSH “Haematology Updates” is published on a quarterly basis and is a quick guide to all the happenings in the haematology community.

To improve the updates, your comments and suggestions are welcome.

We further encourage you to send us write ups and photographs of any PSH event in your city/province and they would be featured in our upcoming updates.

For contact, please refer to our corresponding address.

We hope to hear from you on regular basis.

This updates was designed and edited by:

Mr. Imran Waheed
Coordinator / IT Manager
Off: +92 51 9270076 Ext. 228
Cell: +92 322 5181302
Email: psh.org.pk@gmail.com

CORRESPONDENCE

Dr Mehreen Ali Khan

PSH Secretariat, AFBMTC/NIBMT, Rawalpindi - Pakistan

Telephone: 92 51 9270076 Ext. 207, Mobile: 92 333 5164941

Email: mehreen35@hotmail.com, Web: <https://www.psh.org.pk>