

SUMMARY REPORT of HELP3 team at BMH (DODOMA)

(January 21st to February 8th, 2024)

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Help3 project :

TITLE : Advanced status of training/activity at the first hematologic and “bone marrow transplant” center (BMT) at BMH (Dodoma) to cure children affected with severe hematologic diseases

**** Meeting point : Benjamin MKapa Hospital (BMH) in DODOMA (Tanzania)**

**** Period : November 2023 , January 21th to March 10th - 2024**

**** BMH principal professionals contacted and participants:**

1. Dr. A. Chandika : Executive Director at BMH ; 2. Dr.C.Shija : Assistant Executive Director ;
3. Dr. J.Shakilu : Pediatric Oncologist; 4.Dr. Stella Walanghe , Dr. David and Dr. William : Hematologists; 5 . Dr. Zimbwe : Director of Pharmacy at BMH; 5. Fred Francis Ngiliule :Director of Pathology and Haematology Section 6. Merlikiad : Lab Tecnician at Blood Bank of BMH ; 7. Catherine Aloyce : Lab Tecnician at Microbiology Section at BMH ; 8. Nurses in charge at “BMT UNIT ”;

**** Italian Professionals and other participants**

Haematologists :

**Dr. F. Giglio , Dr. P. Ronchi (20th to 30th November 2023)

**Dr. C. Uderzo , Dr. C. Tassi: (January21st /February8th- 2024

**Nurse: Valeria Tarizzo (January 2024) ;

** Dr. P. Pioltelli (Hematologist) ; C.Airoidi (nurse) (10th of February/25th -2024); Musa Dubali (nurse) 19th to 28th February 2024

** Dr. N.Manna (Hematologist) and F. Sabbatini (Infectious Disease Specialist) 21th of February up to 10th of March

** **Help3 President and collaborator** : Dr. Mario Battafarano; Dr. Edoardo Gomba : 20th to 28th January 2024

**** People contacted and participant outside BMH :**

1. Superior Mother of St. Gemma hospital ,*Sister Eufrasia* ,for solving the following point N°2

2.Our BMH Lab Tecnician , Merlikiad, must go every now and then to St. Gemma hospital in that the diagnostic tool for SCD at BMH (Hb Electrophoresis) is temporarily not functioning . *Sister Fabiola* at St. Gemma Hospital has the same instrument (donated by Help3) and our HELP3 volunteer *Edoardo Gomba* , IT expert, is trying to install in Italy the HbS program on a new computer in order to permit a comprehensive management of the Electrophoresis of Hb at BMH . After the possible installation of the new program ,the new computer will be donated by Help3 to BMH.

2.0 General overview

BMH is an University referral hospital in **DODOMA** for 6 millions of people, having 400 beds capacity , with a School of Medicine, a School of nurses, many Specializations courses including

Pediatrics and, finally an impressive number of facilities able to give in a near future a high level of diagnostic and treatment care for patients affected with malignancies and non-malignancies.

In the area of DODOMA probably more than 2000 new SCD neonates /year (out of 20.000 in all Tanzania) are born , and in the same area more than 500 new cases of childhood Leukemia and Lymphomas a year (out of 4000 in all Tanzania) could be taken into consideration for a specific diagnosis and treatment including BMT.

BMH is now able to offer BMT in pediatric haematological diseases , *mostly in SCD children, as an example of good clinical practice* in the setting of a multidisciplinary activity . Besides that, BMH could serve primarily as referral Center in Tanzania for BMT decreasing the actual expensive “hope trips” to abroad for those few cases who cannot afford the BMT. Other important General Hospitals (Muhimbili, KCMC, BMC...) could start same transplant program and Tanzanian team at BMH will offer all the skills needed to be successful. Even HELP3 Charity (Italy) is moving in the same direction and will be happy to give a support mainly for a specialistic training and scientific improvement.

3.0 Principal aims of the current visits at BMH by Italian professionals:

1) to verify the *status of art* of the ongoing common project previously started since February 2019 in this Hospital with the support of HELP3 Association , and successfully realized since January 2023 with eight BMTs done for the first time in Tanzania .

2) to program some advances for the main needs at BMT Unit of BMH in view of the complex activity concerning the management of severely immunosuppressed patients who will undergo BMT . Italian professionals very expert on the area of BMT have been happy to offer their experience and a specific “on site” training.

3) to plan how to improve those areas (Blood Bank, Hematology Lab, Microbiology Lab...) that are bound to provide more specialistic intervention in view of advanced diagnostic and therapeutic plans.

5) to discuss with BMH Executive Director, *Dr. A. Chandika* , which current and future plans of training /educational/organizational program need to be implemented at BMH

4.0 FOCUS on management of BMT Unit at BMH

4.1 Hematologic and BMT Unit:

Compared to the “startup” of BMTs which took place on January 2023 , the Tanzanian team seems to be more efficient both in quantity and in quality. No matter that the continuous “at distance and on site” second opinion with Italian professionals played an important role.

From the organizational point of view now Tanzanian doctors and nurses have a clear idea on how to manage treatment protocols , how to share opinions/decisions during day and night shift, how to proceed in case of emergency.

Some of the ongoing SOPs /Protocols need to be reviewed and discussed among doctors and nurses' team , just to transfer work modalities one to each other, but especially when there are professionals recently employed. In this sense all the team has been encouraged to set up a "group of Study" , doctors and nurses, able to review for example some of the past Teleconferences prepared by Italian BMT team and constituting an extraordinary tool of refreshment .

Protective environment tools (i.e "Sentinels Air in Plasma Air conditioning" in each of the 4 single bedrooms and the 2 in the corridor of the BMT Unit) dedicated to immunosuppressive patients and equipped by HEPA Filters with microbial destruction, should be properly checked according to the BMH engineers' plan . Most of the BMT staff doesn't know when this specific surveillance takes place.

Written SOPs inside the BMT unit should be available in case of "fire accident".

Written "clinical procedures" on how to clean the entire BMT Unit (at least twice a day) and to avoid infectious complications in immunosuppressed patients will be available at the entrance of each of the patient room

The one or two "storage rooms" available at BMT Unit to keep any kind of items (drugs infusion pumps, scale sterilized vests/gloves, syringes, microtubes, needles for bone marrow aspiration....) should be checked regularly by nurse personnel to replace what is lacking or expired.

The "emergency car" (with written procedures for "in-out" of the needed drugs) and one "defibrillator" for heart failure emergency (with written procedures for the use)and all other instruments needed for support treatment (emergency drugs ,vacuum, aspiration, Oxigen.....) should be checked regularly and there will be a signed prove by who carried out the intervention , what has been used and what must be replaced .

Generally speaking , we've noted a good climate of all participants during the Inpatient BMT Unit rounds and a continuous willing to learn every day .

The Help3 President ,Mario Battafarano, has been present at BMT Unit all the days of his visit and noticed the great commitment of all the professionals involved on the program.

Dr. A. Chandika , BMH Executive Director, has been in contact with both Italian and Tanzanian team, being involved with competence and enthusiasm any time.

The Visit of "Mama SAMIA" President of Tanzania has been emotional and full of real interest for what all the participants to this project were and are able to do. Hopefully "Mama Samia" can support as much as possible new advanced steps we would like to get at BMH.

4.2 What does it need at BMT UNIT (BMH) in the near future :

this important issue has been discussed “face to face” during the visit/mission of Dr. Fabio Giglio and Dr. Paola Ronchi in November 2023 with Dr. A. Chandika and his team involvement .

A main problem emerged on the maintenance of a good replacement of some consumable items at BMH because they are not always available Tanzania (i.e. Central venous lines, Filters in case of RBCs and Platelets transfusions, BM harvesting needles, Blood Bank items...). There is in fact some difficulty to bring the above items from oversea (i.e.from Europe/Italy) to Tanzania because not always it's possible to have on time the due documentation to overcoming *Tanzanian customs*.

A *second point* to underline is the late provision of the above items after a doctor order . In other words, the administrative dedicated BMH personnel should proceed more rapidly both contacting the Tanzanian suppliers , if any, and to receiving back the items.

A comprehensive “outpatient “area to follow the transplanted patients after discharge from BMT Unit *should be set up as soon as possible at BMH*. Because in the future this space could be used by other patients (Leukemic patients for example) one should forecast some minimal/essential characteristics as the following :

- 2 single beds rooms for blood products infusions, chemotherapy.....(+ 1 bathrooms)
- One large common room with 8 beds for IV infusions plus 2 bathrooms (at least)
- 2 rooms for procedures (BM aspiration, lumbar puncture.....)
- 1 Nurse station for preparation of infusions and any kind of procedure (+ Internet/Intranet)
- One protective cabinet to prepare solutions,drugs...
- Storage room (for drugs, consumables items,infusion pumps....)
- Doctors station with Internet/Intranet
- 1 “Play/rest room” for patients and/or parents
- 1 room for “social worker and psychologyst”
- Various (scales, monitors.....)

A comprehensive “Residence” for the patients/relatives should be built soon close to BMH because after discharge from the BMT Unit most of the patients need *constant controls* in “outpatient “ on the first 3 to 4 months after BMT. As a matter of fact , most of the patients are living far away from BMH.

This Residence should be able to host at least ten families (parents and donor + recipient) in “mini apartments”, each one with a little bathroom and possibility to cook ; common laundry should be allowed. A space as playroom is mandatory too.

Help3 will try to give the better support as possible for this new facility.

The experience at BMT Unit of S. Gerardo University hospital in Monza (Italy) and in many similar settings showed a clear advantage for those immunosuppressed patients who must be carefully checked during the follow us

5.0 FOCUS on management of Damu Salama at BMH

5.1 Aims of the visit:

- To meet the personnel working in the Damu Salama, (corresponds to Blood Bank), to understand and eventually supporting interactions among the Blood Bank, the Central Regional Damu Salama, the Laboratory of Hematology and the BMT unit, all involved in the Allogeneic Transplantation Program.
- To ascertain the state of art of quality management in terms of present operating procedures and documents to be implemented or introduced.
- To verify the feasibility of Extracorporeal Photopheresis whether required for transplanted patients affected from acute or chronic graft versus host disease (GVHD)
- To verify the feasibility of Bone Marrow special processing procedures in case of ABO (major and minor) incompatibility between donor and recipient
- To check out that an efficient system should supply the Damu Salama with blood units, devices and reagents routinely employed or exceptionally required.

5.2 Personnel Interviewed: Merlikiad Mhozya MLT, Deogratius Lyimo MLT, Florentina Magesa Nurse, Stephen Temba MLT.

All interviewed were available and greatly collaborative. Personnel is involved in a broad range of activities in the field of blood banking, immunohematology and services to clinical and surgical units operating at the BMH. As regards the BMT program, since 2021-2022 is ongoing a peculiar training, (with onsite support and abroad periods), focused on specific BMT issues: the level of improvement is considerable, and the involved staff express the willingness to progress and introduce new procedures.

5.3 Spaces and equipment's:

The Damu Salama is hosted in an independent building inside the BMH complex, at walking distance from the laboratory department, BMT and other units.

In general spaces are well kept and donor management activities and laboratory procedures are carried out in separated areas.

Separation and other minor manipulation (filtration) of the blood units are done in a wide room where are placed a refrigerated centrifuge, a sterile connector, and a sterile tube sealer, all regularly and periodically inspected and qualified. According to National Health Regulations, validation tests on the collected units are sent to the Central Zone Blood Centre of Dodoma that has in charge the validation of the whole collection and the blood grouping of donors. Units waiting for the validation are stored in a dedicated fridge whose working temperature is continuously kept under control.

Bloodproducts Xray-irradiator (RADGIL-GILARDONI) is placed in a separated and refrigerated room; platelets and PRC are irradiated for allotransplanted patients or appropriate cases, on request by BMT or other Units.

A **cell separator OPTIA Spectra Terumo** is available for several procedures:

1. Platelet apheresis on donor's call
2. Erythro-Exchange (EEX) in SCD or other patients
3. Therapeutic Plasmapheresis
4. Manipulation of stem cells collected in Bone Marrow *
5. Collections of lymphocytes from peripheral blood to ECP purpose *

** Procedures at point 4 and 5 are not yet carried out routinely, but the feasibility has been verified in this visit*

The **UVA PIT system** *to be used in case of refractory GVHD* is a closed, offline system to UVA irradiate Lymphocyte collection after addition of 8 Methoxypsoralen, with ECP (Extracorporeal Photopheresis) purpose* not in use routinely.

5.4 Present Activities

1. Blood products collection, Insite and out reach
2. Whole blood separation into blood products
3. Blood products irradiation, on specific request
4. Blood products filtration by mean of bed-side filters, on specific request
5. Storage of locally harvested units and apheresis platelets
6. Units supply to the Laboratory of Hematology that receives all patients' transfusion requests and performs pre-transfusion and compatibility tests.

5.5 Quality Management:

National Blood Service of Tanzania has published and updated Operating Procedures, Operating Instructions on every topic in the Transfusion and Immunohematology Medicine field. Nurse *Florentina Magesa* is the Quality Manager : procedures, evidence recording sheets and eventual qualification documents are stored in specific files, kept in closets at the Damu Salama. Specific procedures on immunohematology issues and adherent to AABB Standards are recorded in the Hematology Laboratory.

5.6 Strengths points

- Personnel proficiency
- Availability of spaces and equipment
- National Informative system for Donors and Donations traceability currently in use
- Platelet apheresis collection
- Capability to separate whole blood.
- Capability to irradiate blood products

- Capability to filter
- Availability of Erythroexchange (EEX) procedures
- Good documental recording

5.7 Items to improve

- Overload of work. Despite the good level of qualification of the personnel employed in the facility, nevertheless a true overload of work it is evident due in part to the lack of personnel and to the amount of work to carry out even outside the Damu Salama. *At least three qualified persons in every task are strongly recommended to ensure the continuity of activities*
- Difficult availability of compatible blood from Volunteer Not Paid Donors to regularly have the due support “on time” and in particular, to maintain a constant support of blood products needed to favor a safe post BMT phase to all the transplanted patients. This is a specific task of the Central Zone Blood Centre of Dodoma, however, campaign to promote blood donation must also be sponsored by the peripheral collection centers.
- Not always available three cells panels and absence of extensive 11 cells panels to detect the specificity of alloantibodies in recipients of blood units or bone marrow: these tests are of capital importance and must be in use to reinforce safety of transfusion
- The availability of Feno typified units for minor Red Cells antigens might reduce the waiting time for finding a compatible unit in case of alloantibodies detection in patients. This activity should be carried out at the Central Zone Blood Centre or at the Hematology Laboratory.
- Difficult supply of reagents and peculiar devices. *Research* for local or zonal distributors must be implemented to reduce costs and accelerate time of supply
- Improve the supervision of stocked materials to avoid both the permanence of expired devices in the store and the risk of incorrect counts of usable materials. Stock cards and informative system are employed at the general laboratory store of the BMH, but it would be advisable to have a person in charge at the BMH Damu Sama who keeps under control the storage status of materials in use.
- Interactions with the clinical unit BMT are ongoing. However, it’s strongly recommended strengthening communications by regularly planned meeting and by written forms or documents when required, to program in advance procedures or exams for special patients as in the following cases:
 - Alloimmunized subjects
 - ABO incompatibility between Bone Marrow donor and recipient requiring the isoagglutinin’s research test
 - Patients showing a refractoriness to platelets’ transfusion
 - Patients in need of EEX in preparation to ALLOBMT or for clinical reasons

6.0 Challenges of particular relevance for Damu Salama related the BMT program

6.1 ABO incompatibility between Donor and Recipient

This is a challenging issue and sometimes it might require the Graft manipulation or plasmapheresis procedures pre graft infusion in patients showing high Isoagglutinin's titration. Nevertheless, Graft manipulation, consisting in red cells depletion by manual or automatic procedures, is a critical process. In real local conditions, manual red cells depletion is unaffordable due to the risks of losing stem cells and/or infecting the graft. On the other hand, automatic manipulation by the OPTIA Spectra machinery it is feasible but might be difficult for technical motivations in small, harvested volumes. In conclusion, from the published data and after a consultation with highly experienced in processing bone marrow colleagues, one suggests doing a specific risk analysis on this issue to make the decision that best protect the integrity of the harvests and the safety of the recipients. In any case the isoagglutinin's research is mandatory for every ABO incompatible couple donor-recipient.

6.2 Bone Marrow manipulation

A mock procedure has been carried out just to familiarize with the process and to focus on specific technical issues.

6.3 ECP (Extracorporeal Photopheresis)

Several ECP treatments are needed in case of post-BMT acute or chronic "graft vs host disease" not well responding to standard immunosuppressive therapy. The off-line ECP consists of a previous collection of lymphocytes from the patient by the OPTIA Spectra machinery, then a rapid incubation of the harvest with the UVA sensitizing drug 8-Methossipsoralene, followed by the UVA irradiation in a special machinery, PIT UVA System, available at the BMH Damu Salama. The responses are usually really good, but at the moment, the most relevant problem would come from the rare request for these multiple procedures that are in general quite urgent, so far that the management would be difficult in particular due to the risks that some expired materials could be unusable at the moment of the beginning of the therapy and the not very experienced personnel in carrying out all the process. In any case, if needed, a planned at distance assistance might be available .

6.4 Lymphocyte collection from peripheral blood

A mock procedure has been carried out just to familiarize with the process and to focus on specific technical issues on Lymphocyte collection from peripheral blood

6.5 UVA Irradiation by PIT UVA SYSTEM

A mock procedure has been carried out just to familiarize with the process and to focus on specific technical issues

7.0 FOCUS on future commitments by HELP3 and BMH

7.1 *Diagnosis and treatment of malignant and nonmalignant diseases in Tanzania .*

One forecasts a high number both of **Leukemias** and **Lymphomas** in Tanzanian children. Considering the high number of the births a year in this Country (4-5 children per family) and a similar incidence of children affected with the two above malignant diseases as in Europe (around 40 to 50 children per million of children each year) , *it is possible to forecast in Tanzania at least 2000 new diagnosed Leukemias a year and 2500 new diagnosed Lymphomas a year.*

Therefore there is a high demand of Hematologic Centers to be involved in this area.

BMH authorities should consider a comprehensive diagnostic and treatment plan in children affected by the above diseases ; one example is AML (acute myeloid Leukemia) whose prognosis is very bad (100% of mortality in LICs) but once the patients receive the “first line therapy” in Tanzania and obtain a complete/durable hematological remission they could undergo a subsequent BMT according to consolidate eligibility criteria: the AML transplanted patients will have a 80% of Leukemia free survival as claimed by recent Literature.

The team of doctors and nurses at Hematologic and BMT Unit of BMH will be prepare a plan of possible allogeneic transplants in those hematologic patients who need this therapy . As a matter of fact, it is possible to apply a BMT approach similar to that employed for SCD children.

7.2 Even **Severe aplastic anemia** patients may be considered eligible for BMT and because there is a high incidence of this disease in all Tanzania , the transplant approach is fully justified.

Now the mortality rate for the above disease is very high (around 90%) without transplant, while an HLA identical sibling donor transplantation can provide a more propre and durable overall cure rate (around 85-90%) .

7.3 Training and capacity building toward Hematology Lab at BMH :

The majorities of suspected cases of hematologic malignant diseases need today a complete and correct diagnosis thanks to a modern instrument , so-called **Flowcytometry** which is available at BMH, *but there is an urgent need to train one professional on the interpretation of the data .*

*Help3 is fully involved in hosting a Lab Technician (probably **Deogratius Vincent Lyimo**) for at least one month of training in a good Hematologic Lab in Italy on the course of 2024*

7.4 Training and capacity building to implement Pharmacy activity in favor of BMT and Hematologic Unit

Even if at present time the BMH Pharmacy is more than sufficient to cope with a comprehensive plan aimed at procuring ,managing and distribution of the essential drugs , there is a need that the **Dr. Zimbwe** , already a high level Pharmacist , can have an extra training in Italy (i.e at St. Raphael University Hospital -Milan) to approach the modern knowledges in this field including both the pharmacokinetics /the bioavailability and the risk /benefit of the new drugs used in the area of Chemotherapy or BMT (for example use of Car-T after BMT) .

Help3 is more than happy to give this opportunity of training to Dr. Zimbwe in Italy on 2024

7.5 Clinical research

Since the beginning of this extraordinary experience , HELP3 has been very interested in favoring research at BMT Unit . The Tanzanian team could be supported by Italian team from the scientific point of view to publish * case reports * , *overview* and *clinical studies* of their experience on BMT for SCD; even the Tanzanian nurses' team should start same activities with the aim to increase their knowledge level and spread out to other colleagues in the Country what they learnt.

The scientific contribution should then be published on important medical Journals as significative experience in all the Sub-Saharan area.