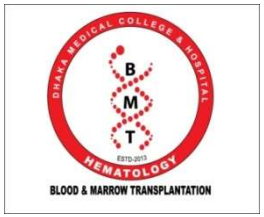
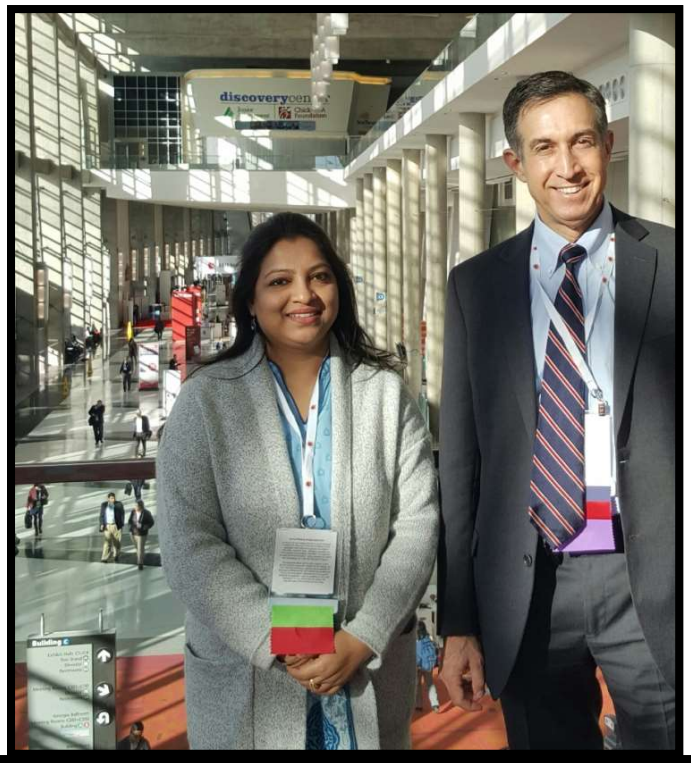
Infectious Complications during Bone Marrow Transplantation: our experience

Dr Mafruha Akter FCPS
Associate Professor
Dept of Hematology
Dhaka Medical College Hospital
Dhaka



No Conflict of disclosure


DMCH




MGH
1811
LUNDER BUILDING
MASSACHUSETTS GENERAL HOSPITAL
ENTRANCE
ENTRANCE
EMERGENCY

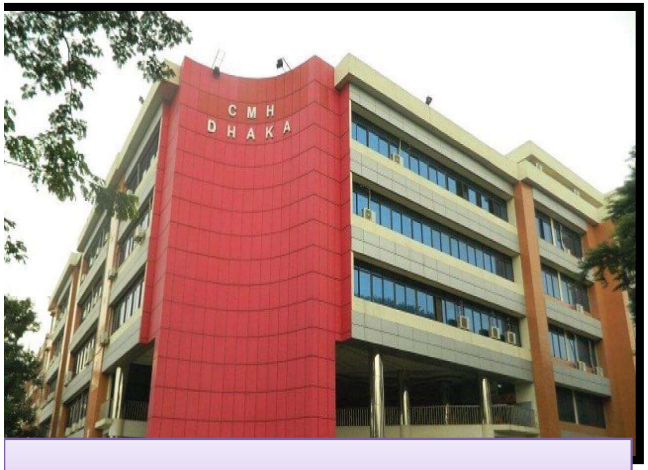

Ucla
BRUINS
UNIVERSITY OF
CALIFORNIA LA

5 HSCT centres of Bangladesh

(Chronology According To Establishment)

1 Dhaka Medical College Hospital (DMCH) 2014

2 Evercare Hospital Dhaka 2016



3 CMH Dhaka 2016

4. BSMMU 2018

5.Asgar A Hospital 2020

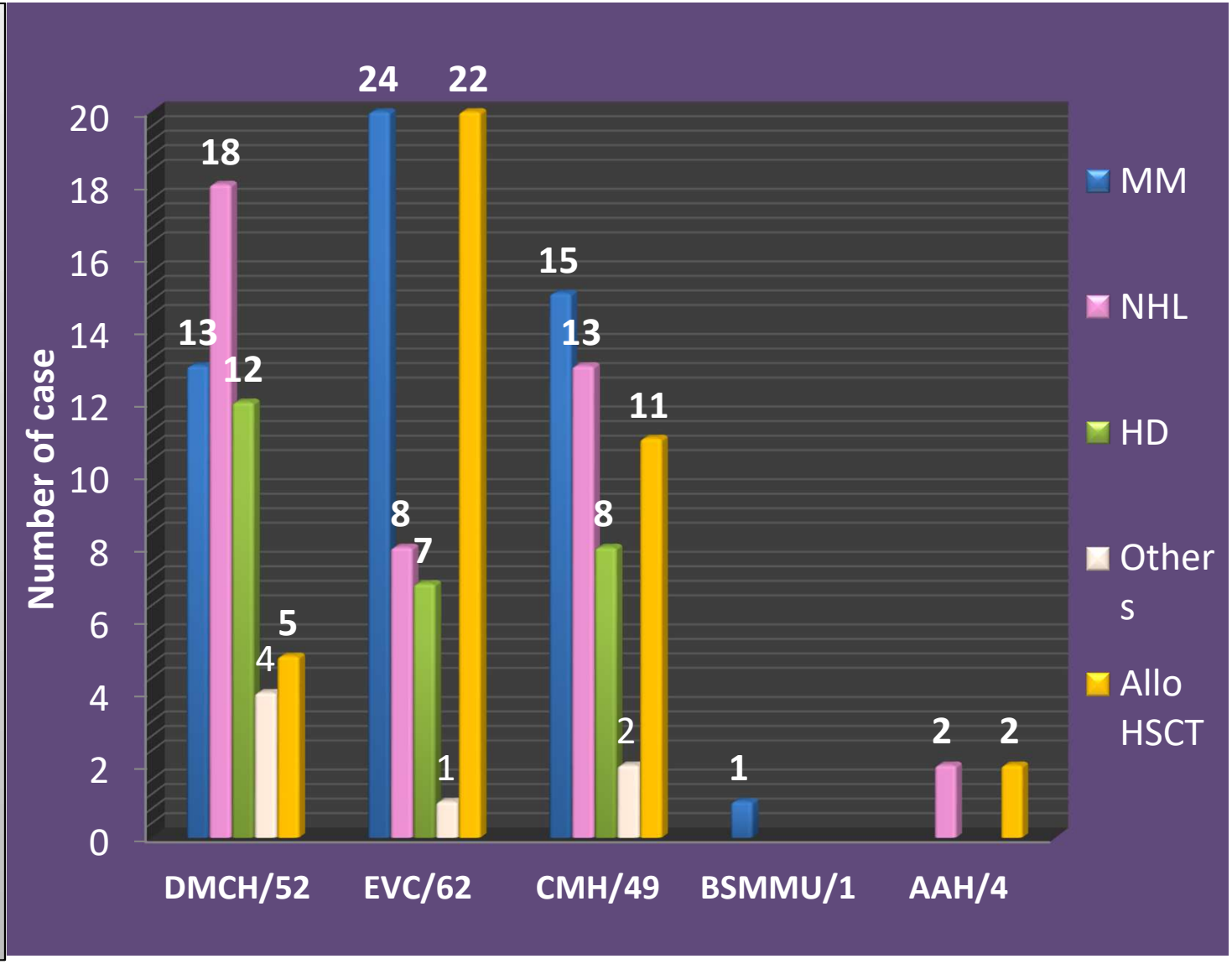
Centre wise Transplant activity

- Average age 39.4Y (15-69 Yrs)
- M:F=3:1

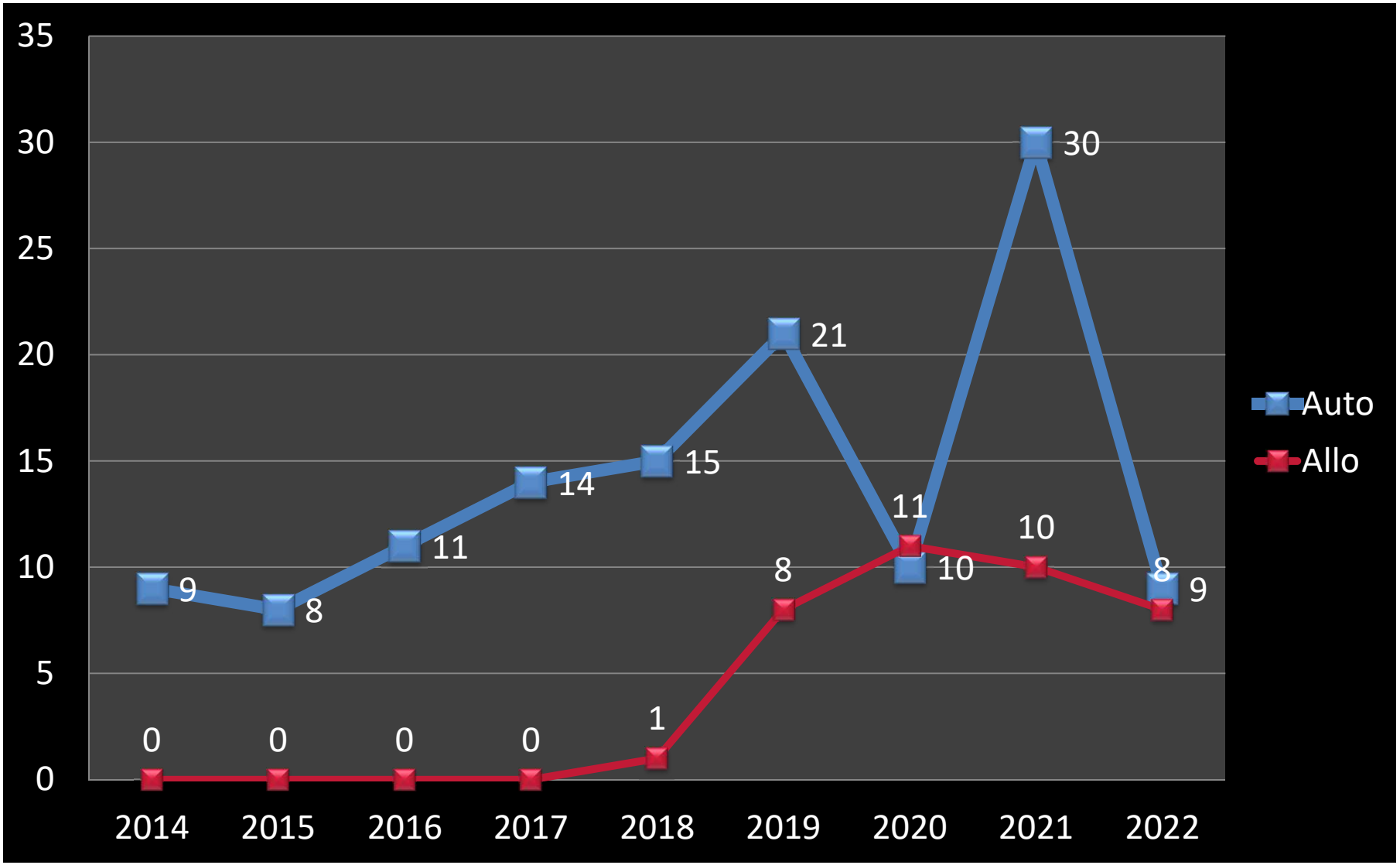
- MM=53
- NHL=41
- HL=27
- Others=07
- Allo HSCT =39

- Engraftment:
  N D+11
  Plt D+12

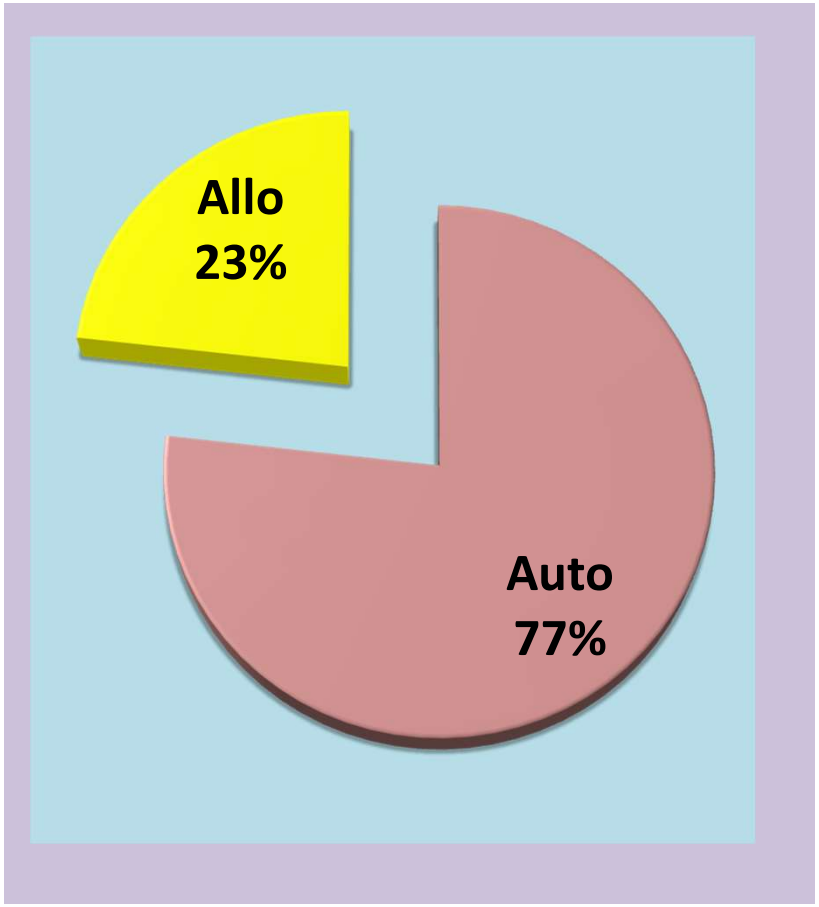
- TRM 0% in Auto
- TRM 15% in Allo

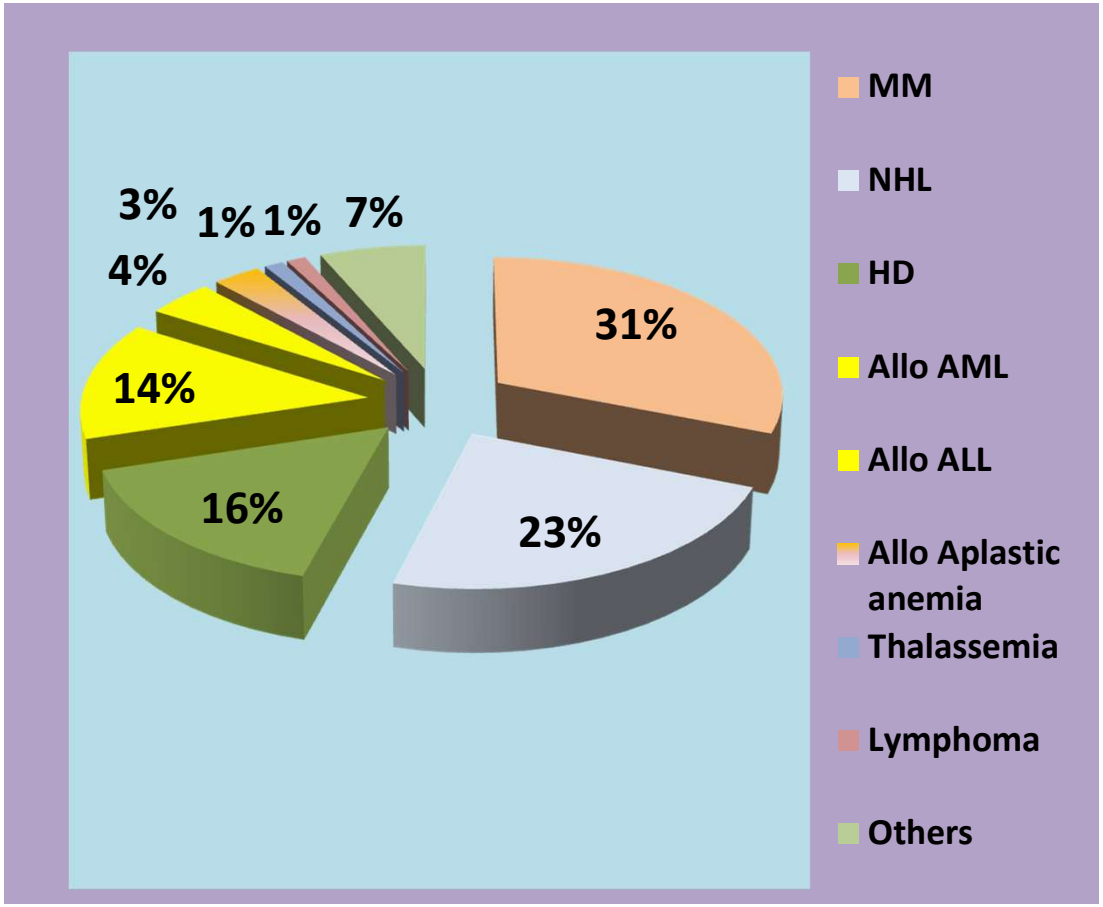


Transplant activity by year in Bangladesh since 2014



Overall Status of HSCT of Bangladesh (n=168, Auto =129, Allo =39)





Complications of HSCT

Autologus :

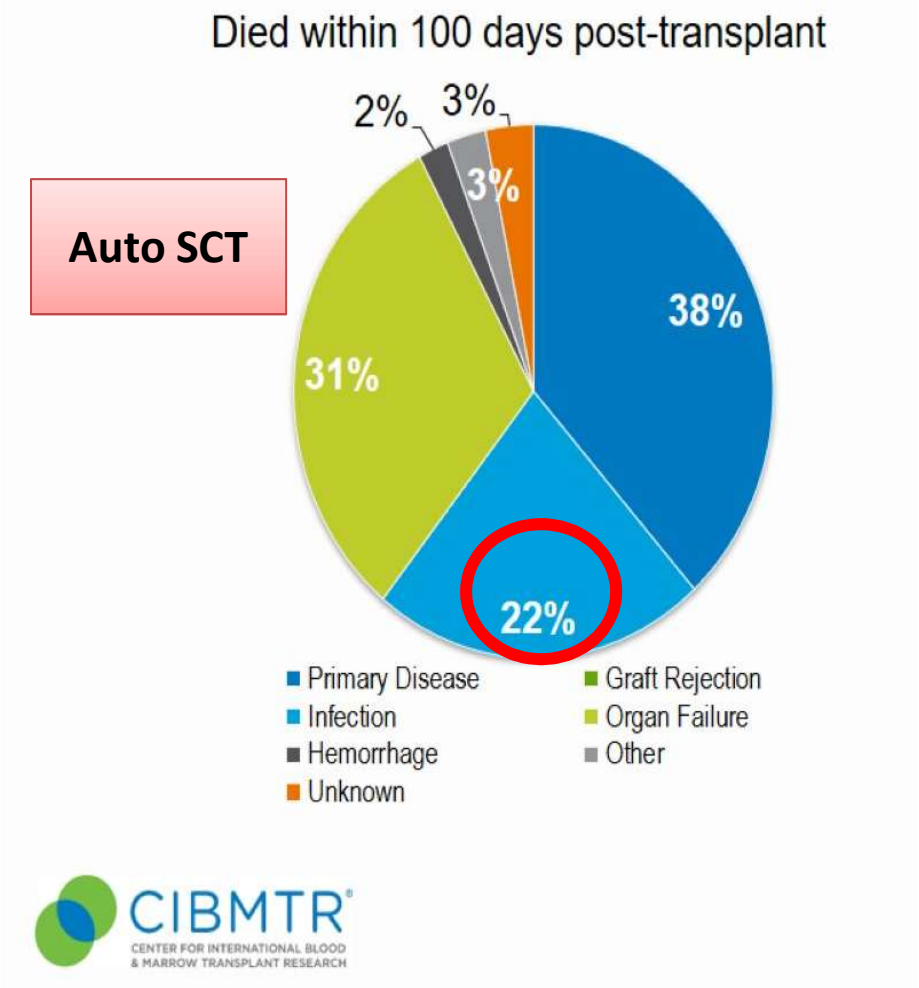
- **Early : < 100 D**
  - ***Infection***
  - *Bleeding*
  - *Organ toxicity*
  - *Others*
- **Late: > 100D**
  - *Relapse*
  - ***Infection***
  - *Gonadal failure*
  - *Secondary malignancy*
  - *Organ toxicity*

Allogeneic :

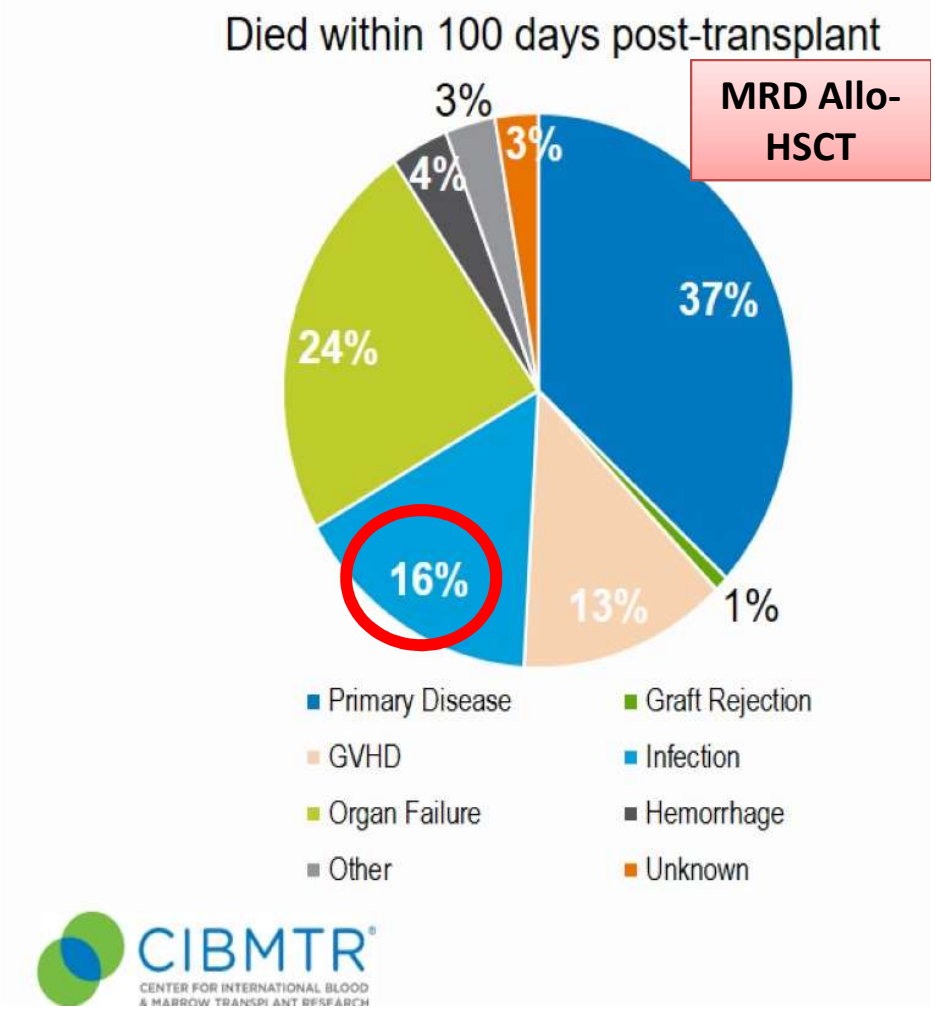
- **Early :**
  - ***Infection***
  - ***aGVHD***
  - *Bleeding*
  - *Organ toxicity*
  - ***Graft failure***
  - *Others*
- **Late: :**
  - ***Ch GVHD***
  - *Relapse*
  - ***Infection***
  - *Gonadal failure*
  - *Secondary malignancy*
  - *Organ toxicity*

Cause of early death >18 years with HSCT in 2018-19 in USA

Auto SCT



MRD Allo-HSCT



Timeline of transplant and infection

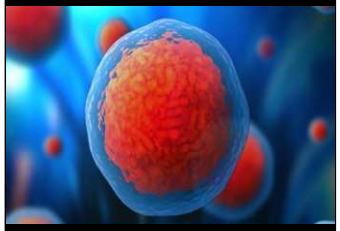
5 – 10 Days Prior

Day 0

Weeks

Conditioning Period

Stem Cell Infusion



Timeline of transplant and infection

Bacteria , Fungus, HSV etc

5 – 10 Days Prior

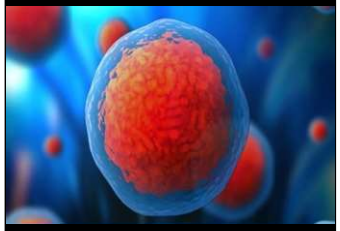
Day 0

Day 12 - 15

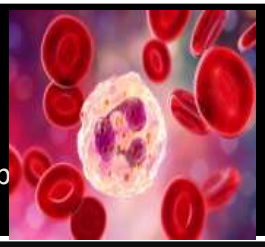
Day 20 ++

Conditioning Period

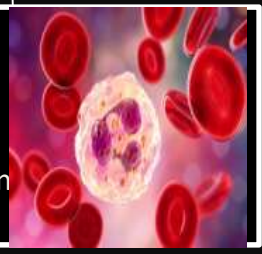
Stem Cell Infusion



Neutrophil Recovery (autologous transp



Neutrophil Recovery (allogenic transplan



Timeline of transplant and infection

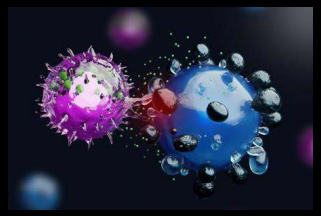
Aspergillous , CMV, HZV, EVB, Pneumocystis

Steroid, GVHD, Cyclosporine, Tacro

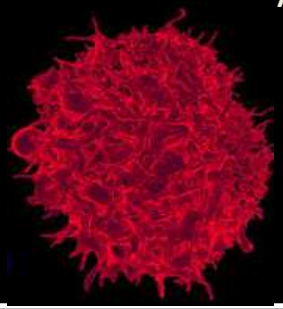
Weeks - Months

Months to years

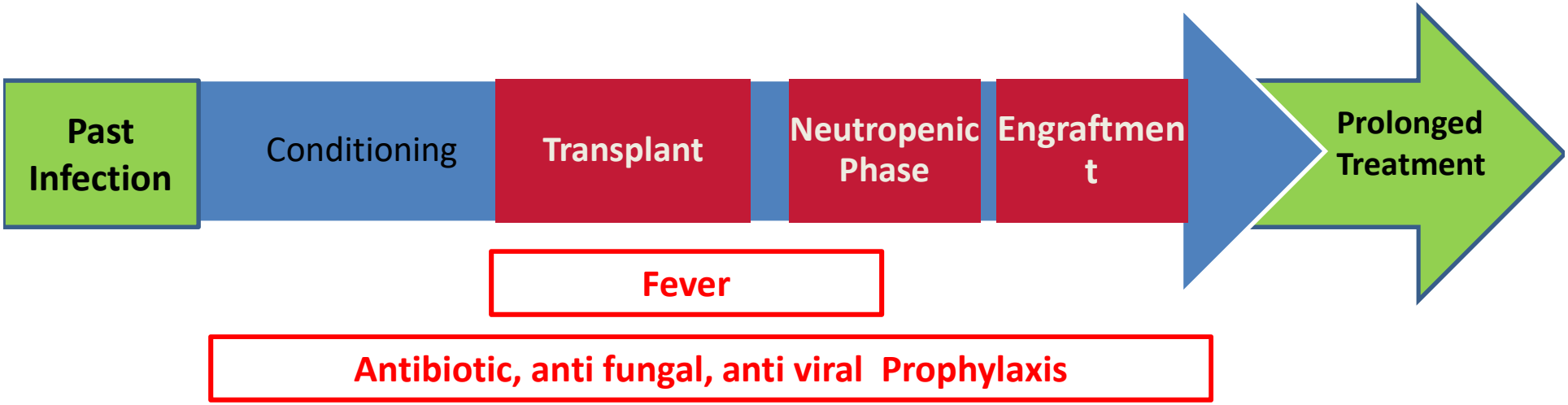
NK Cell Recovery

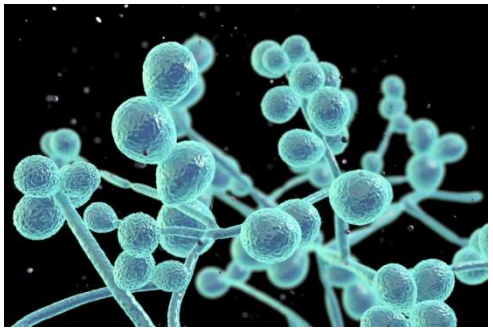


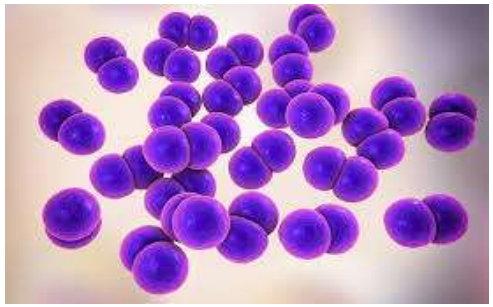
T – cell Recovery

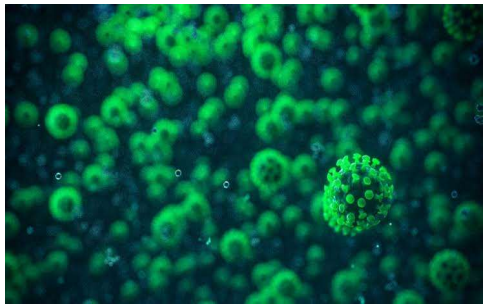


Timing of Antimicrobial Therapy
Post - HSCT









Case # 1
Neutropenic sepsis

- An 19 year male > BEAM+Auto HSCT, for relapsed DLBCL> D0 uneventful>
- D+1 : abdominal cramp, tenderness+, oral & gut mucositis GII, loose stool 10 times/day. NO Fever> worsened to sepsis
- What to do now with antibiotic stewardship?

Initial management of fever with nutropenia

Clinical assessment

diagnostics

- two sets of blood CS (CV line and peripheral blood)
- Urine CS
- Any other swab
- Stool for C diff toxin
- Radiological test: Xrays, CT scan

Empiric antibiotic

Cefepime

Carbapenem

Piperacilline-Tazobactum

1 hour

Re- asseess

72-96 hrs

Unstable, fever

Search focus

Change antibiotic, add aminoglycosides

Antimold

Stable, fever

Search focus

No change

Antifungal

Stable ,no fever

De escalate

Open Forum Infectious Diseases
MAJOR ARTICLE

Early Antimicrobial De-escalation and Stewardship in Adult Hematopoietic Stem Cell Transplantation Recipients: Retrospective Review

Matthew Snyder,[1] Yanina Pasikhova,[1] and Aliyah Baluch[2]

Departments of [1]Pharmacy and [2]Infectious Diseases, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida

Background. Antimicrobial stewardship in allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients remains underutilized in North America. European guidelines advise de-escalation of broad-spectrum therapy after 72 hours in select patients with neutropenic fever of unknown origin. This is not commonplace in the United States, as current guidelines recommend broad-spectrum therapy until neutrophil engraftment. If de-escalating after at least 5 days of broad-spectrum therapy and defervescence in neutropenic allo-HSCT recipients does not predispose them to recurrent fever or infection, the practice could afford several

De –escalation strategy:

- upfront combination, targeting MDR> de-escalated if MDR is not detected.
- Whom: High risk for MDR
- Adv: Lower mortality
- Dis Adv: high abx pressure

Escalation strategy:

- Start with monotherapy> then add 2nd
- Many patients
- Adv: less use, less toxicity
- Dis Adv: MDR , early death

Algorithm for neutropenic patient in HSCT

<u>CASE 1: Neutropenic sepsis:</u>

- **responded well clinically with initial combination(Cefepime+ Vanc+ Metro)**

- Blood, Urine, stool CS: No growth
- Stool for C diff: negative

- Kept on same antibiotic with **<u>de escalation gradually</u>**

- Engrafted on D+9
- Cured from lymphoma 9 years

Persistent fever !

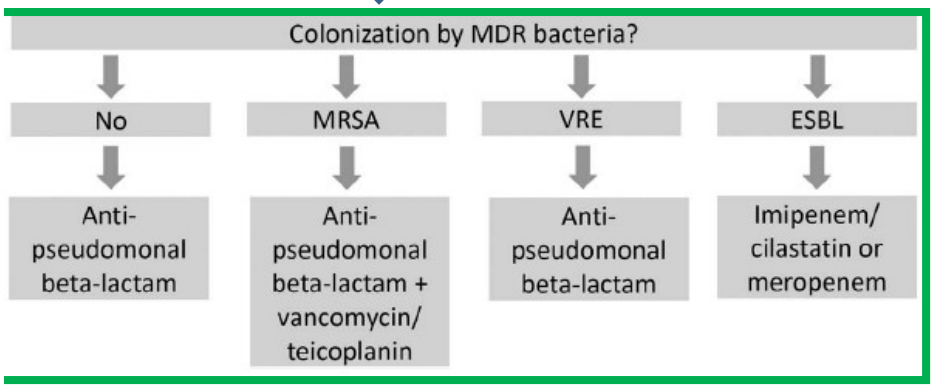
Unstable, fever> 72 hrs

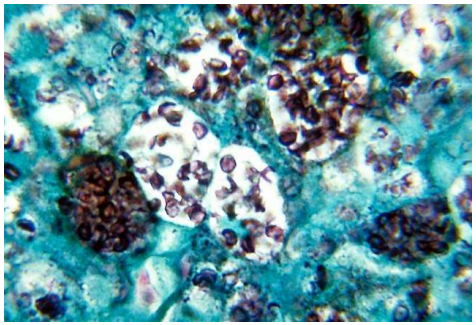
Search focus

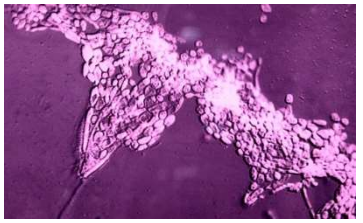
Change antibiotic, add aminoglycosides

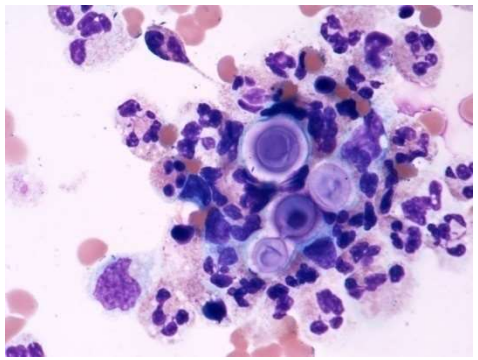
Antimold

Invasive fungal infection?
Broaden antifungal
pre-emptive
Or empirical









Case 2# Hematuria in AutoSCT
Rare

- 49 Y male of rMM> **ASCT with HDM**> **on D+6 red urine** /frank blood, dysuria, urgency, frequency, hesitancy
- Mild loin pain & fever & neutropenia
- Platelet: 60K
- Coagulation work up :N
- work up for infection: negative
- renal function: WNL
- Antibiotics & supportive care
- Transfusion of platelet & RCC
- Red urine continued> Hemorrhagic cystitis

CMV Virus load in urine

Case #2 issue: HC due to CMV

- 49 Y male of rMM> ASCT with HDM> on D+6 red urine /frank blood, dysuria, urgency, frequency, hesitency
- Mild loin pain & fever>
- Platelet: 60K
- Coagulation work up :N
- work up for infection: negative
- renal function: WNL
- Antibiotics & supportive care
- Transfusion RCC, Plt
- Red urine continued

- Bladder irrigation
- Still red urine, dysuria>
- Engraftment on D+8 & D+11
- Viral work up from urine
- **CMV Ag + in Urine by PCR on D+13**
- **Gancyclovir added**
- CMV titre reduced in urine
- CMV neg D+25
- Patient is still in CR with good QoL.

Post HSCT Viral infection

Reactivation:

- CMV
- HSV
- HHV-6, HHV-7, HHV-8
- EBV
- VZV
- BK V

Sporadic:

- Adenovirus
- Influenza V, ParaInfluenza
- Hepatitis V
- Noro Virus
- COVID 19

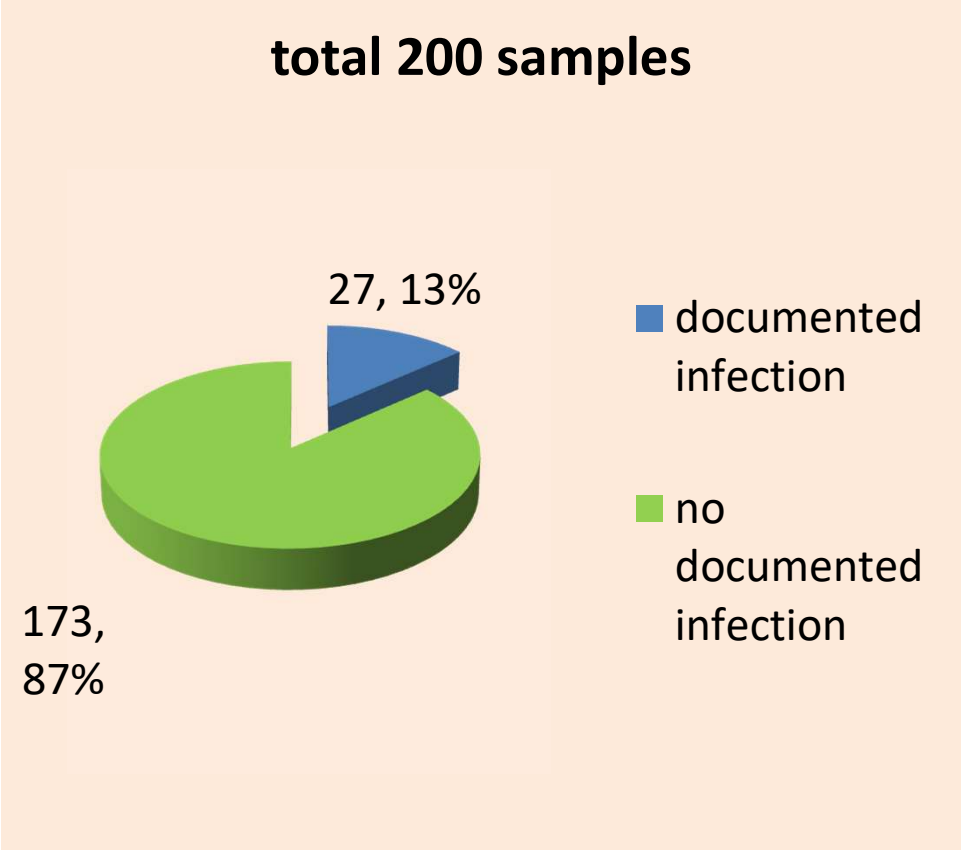
CMV:

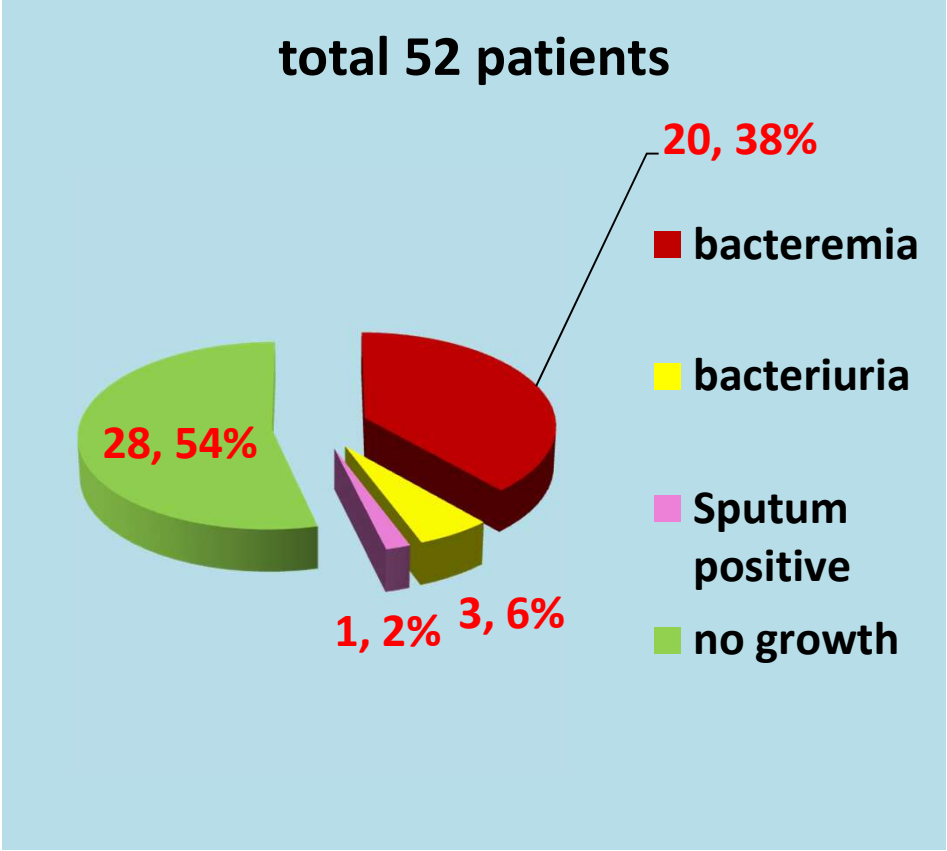
- Most significant infection
- TBI, MAC, chGVHD
- **Pneumonia, enteritis,hepatitis, retinitis, encephalitis**
- CMV pneumonia: 10-30% AlloHSCT
- CMV end organ disease : 80% in CBT
- Therapy:
  - Gancyclovir
  - Valgancyclovir
  - Foscarnet

Post transplant infection in DMCH

- Total 52 cases in DMCH
- 98% had neutropenic fever
- 200 samples (blood, urine, stool and others) for culture and sensitivity
- 27(13.5%) samples from 24 patients were positive for organisms.
- Multidrug resistant bacteria 60%

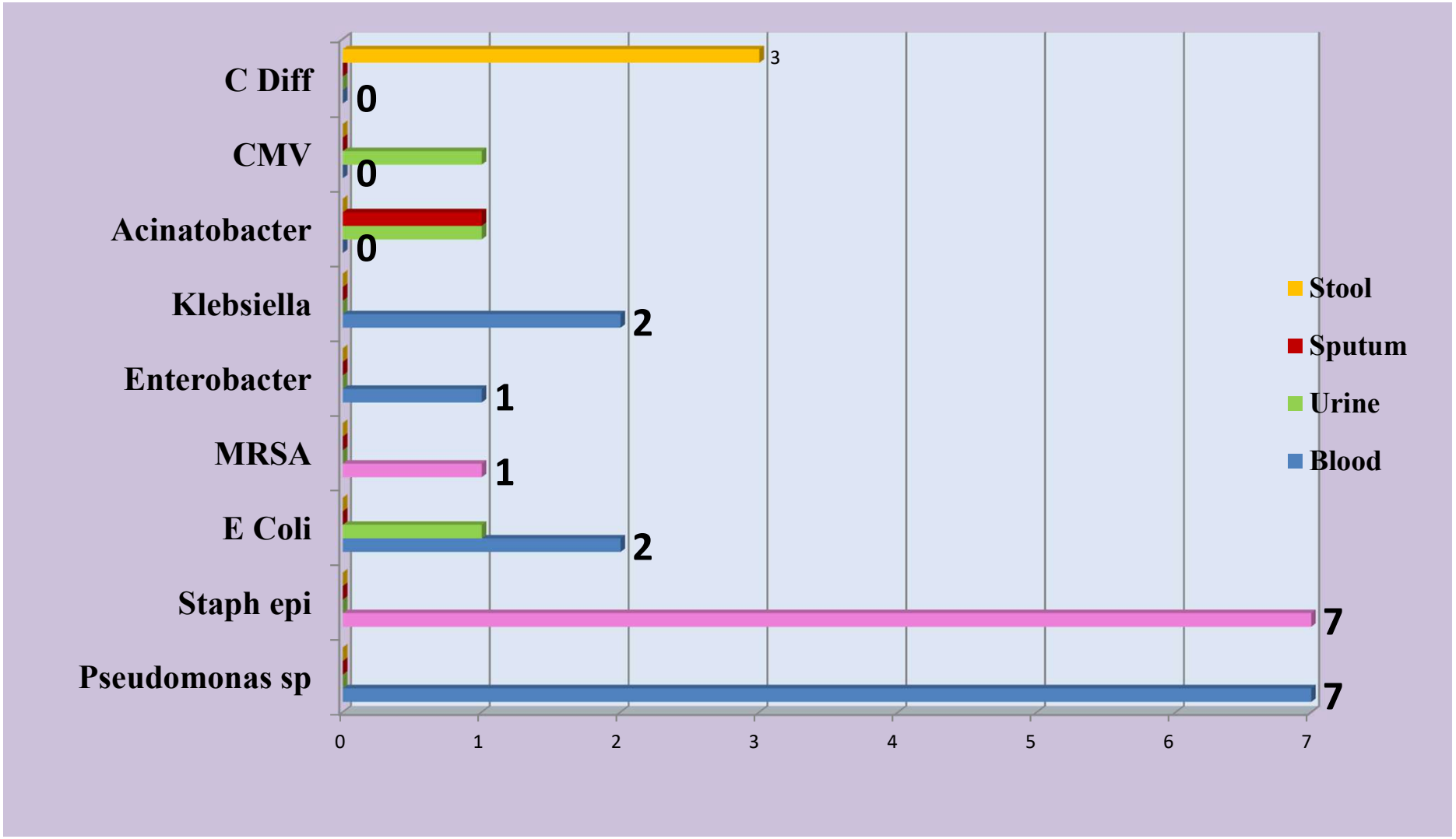
27 samples from 24 individuals were positive





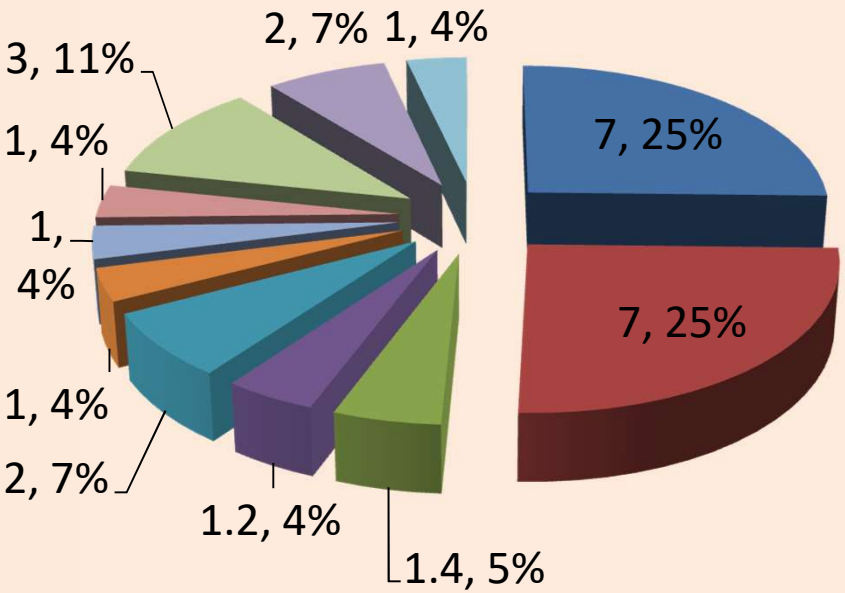
DMCH HSCT infection

Gram negative 75%> Gram positive 25%

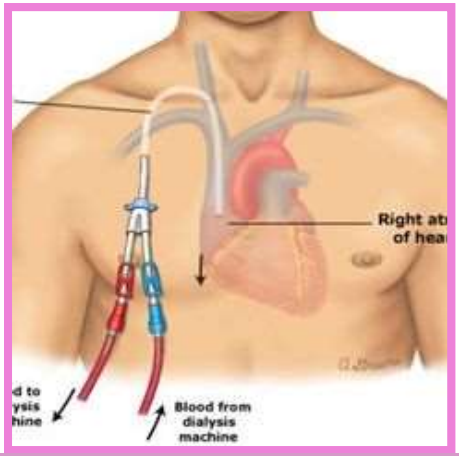


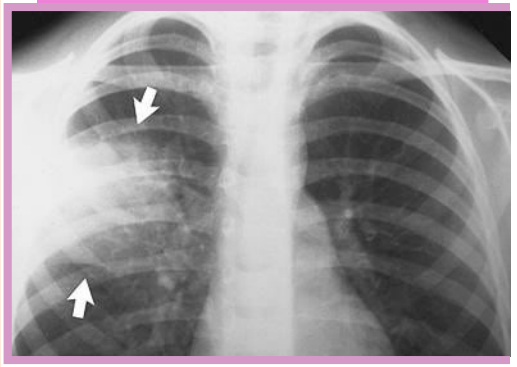
Focus of infection may be anywhere

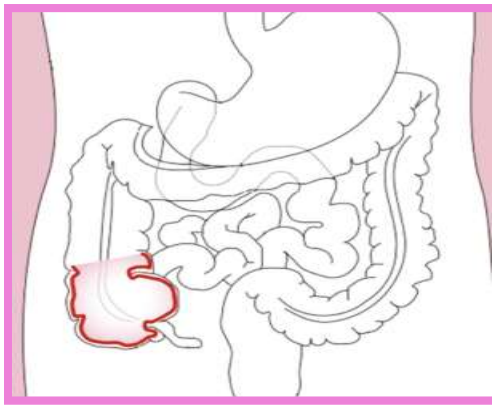
Organisms identified in 45% patients.
60% MDR



- Pseudomonas
- Staph Epidermidis
- E Coli
- MRSA
- Klebsiella
- Enterobacter
- CMV Cystitis
- Sputum Acinator
- C Diff in Stool
- E Coli Urine







Post Transplant Infection in Evercare Hospital

- As of 2022, total 60 HSCT(20 Allo HSCT). Now 72.
- <u>Allo HSCT:</u>
  - 25 % documented bacterial infection in Allo HSCT
  - E. coli and Clostridium difficile most common.
  - Post engraftment viral infection 50%, mostly CMV.
- <u>Auto HSCT:</u>
  - Clostridium difficile most common.
- TRM due to infection 10%

Conclusion

- Infection is the leading cause of NRM.
- 45% documented infection in DMCH, 20-50% in EVC.
- Post transplant infection is multifactorial.
- Broad spectrum antibiotic is needed in 1st hour.
- Bacterial infections are more common.
- Gram negative > Gram positive (75%> 25%)
- Fungal and viral documented infection are less.

Further reading

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- AUTHOR=Chang Ying-Jun, Zhao Xiang-Yu, Huang Xiao-Jun TITLE=Strategies for Enhancing and Preserving Anti-leukemia Effects Without Aggravating Graft-Versus-Host Disease
- Many more

DHAKA MEDICAL COLLEGE & HOSPITAL
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HEMATOLOGY
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THANK YOU