

**Availability of diagnostics and  
treatment modalities for hepatitis B  
in Albania.**

**Experiences of Infectious Disease  
Service**

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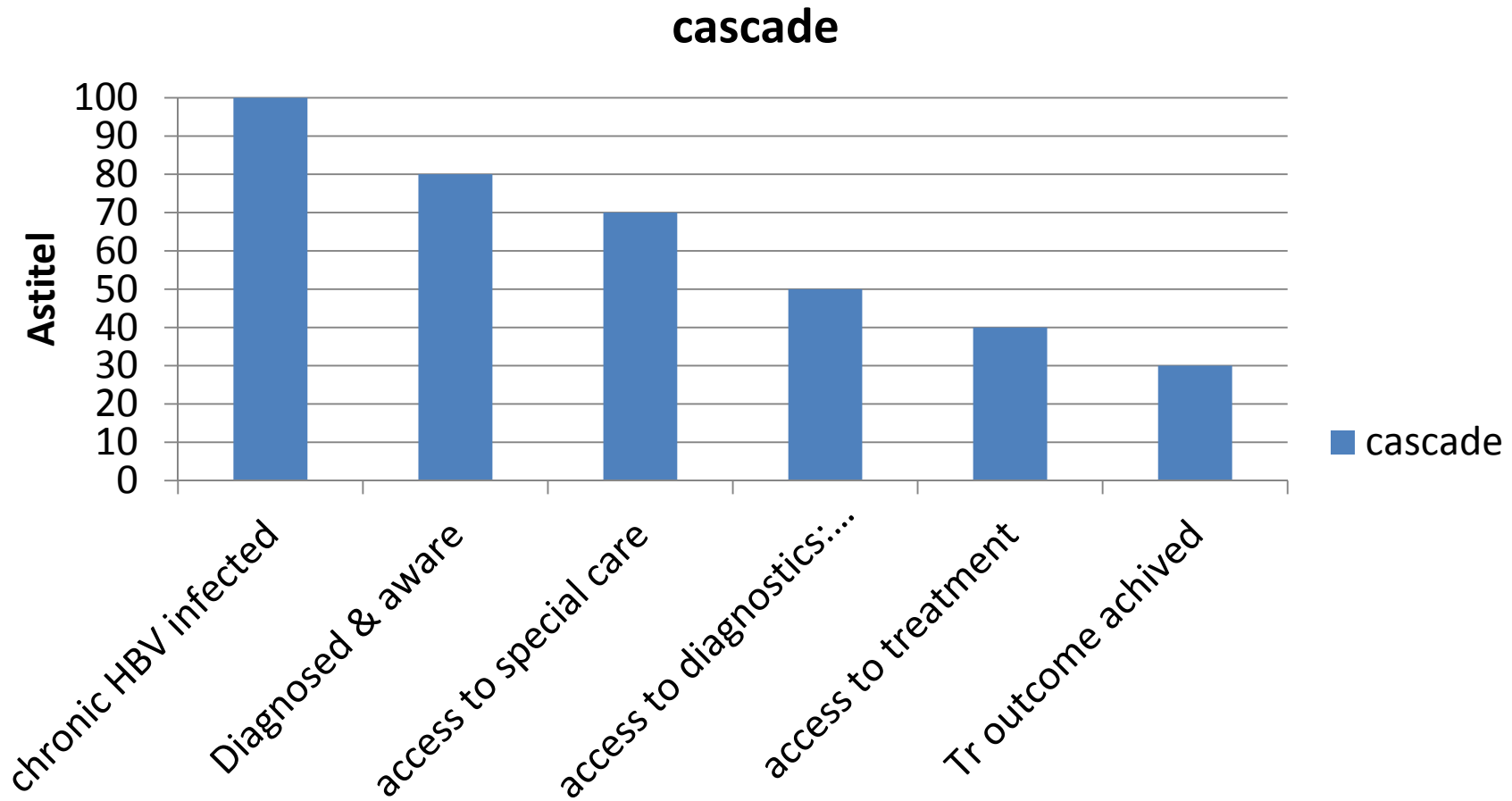
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# Outline

- Review of some epidemiological aspects and HBV treatment cascade needs in Albania
- Diagnostic and treatment modalities assessment (according to EASL standards)
- Data on TDF treatment at the cohort of HBV patients followed at ID Service, UHC Tirana (CHB, severe HBV, reactivated CHB)

# Cascade of care for HBV (no data)



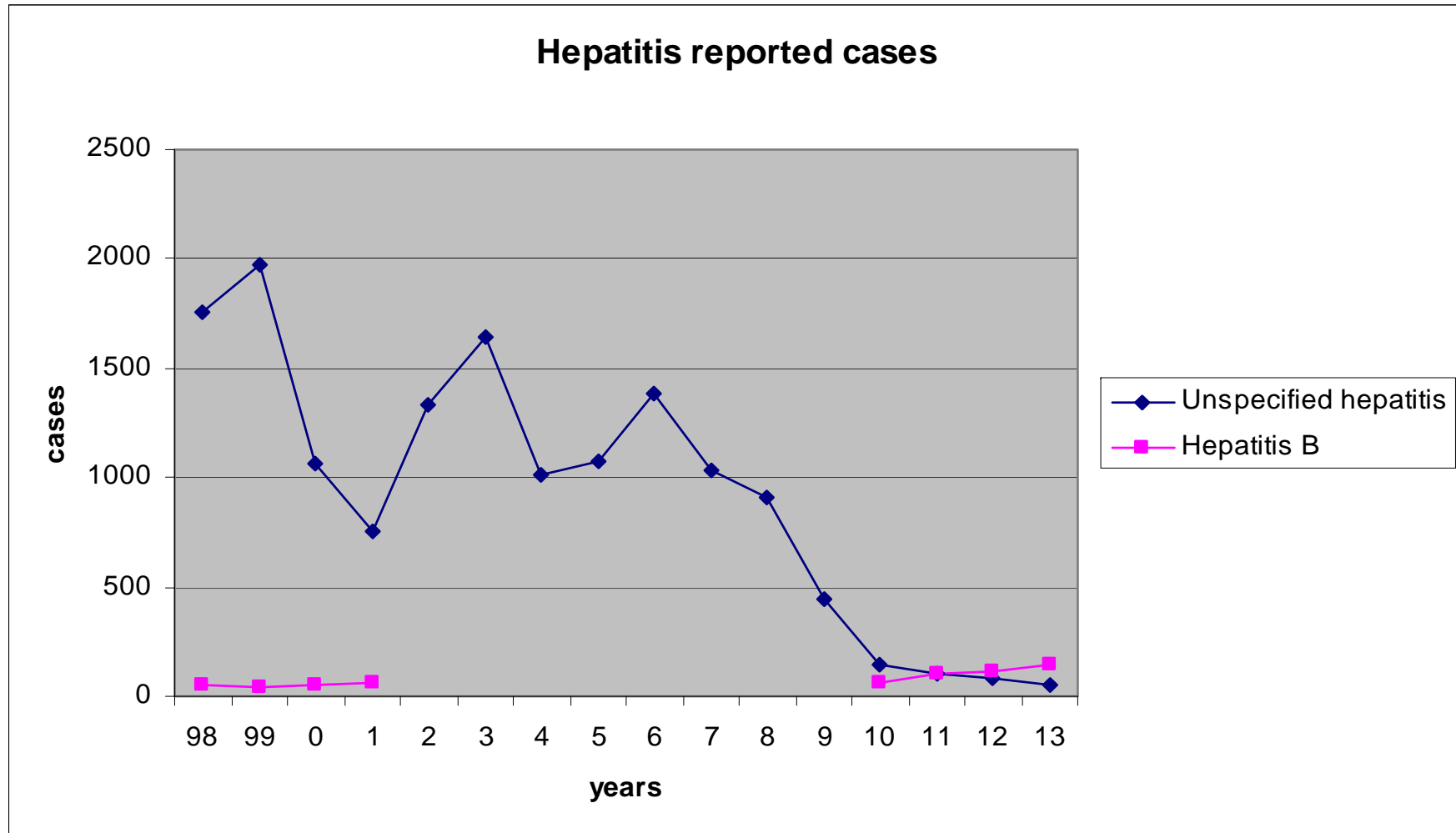
## Sero-prevalence studies of HbsAg among Albanians , 1990-2009

Nr	Author	Year	Study area	Target/age	Sample size	% prevalence HbsAg
1	Roussos A et al	90'	Greece, Athens	Albanian refugees, adults, Greece	76	22.4%
2	Santantonio T. et al	93	Italy	Albanian refugees, all ages, Italy	393	19%
3	Dalekos GN. et al	90'	Greece	Albanian refugees, all ages, Greece	1025	22.2%
4	Milionis C	90'	Greece	Albanian refugees, adults	504	11.7%
5	Chirona M. et al	97	Italy	Albanian refugees, all ages, Italy	670	13.7%
6	Malamitsi-Puchner et al	1996	Greece	Albanian refugees, pregnant women, Greece	500	13.4%
7	Papaevangelou V. et al	2003	Greece	Albanian refugees, pregnant women, Greece	409	9.8%
8	Duro V, Qyra Sh	1999-2009	Albania	Blood donors	79274	7.9%
9	Elefsiniotis IS, et al	2003-04	Greece	Albanian refugees, women reproductive age	2040	4.9%
10	Resuli B, et al	2004-06	Albania	Adults, different groups (total) Pregnant women	3880, 640	9.5% (total) 7.3% (preg wom)
11	Katsanos KH, et al	2006	Greece	Albanian refugees, all ages, Greece	410	11.8%
12	Duro V et al	2004-08	Albania	Blood donors	52727	6.7%

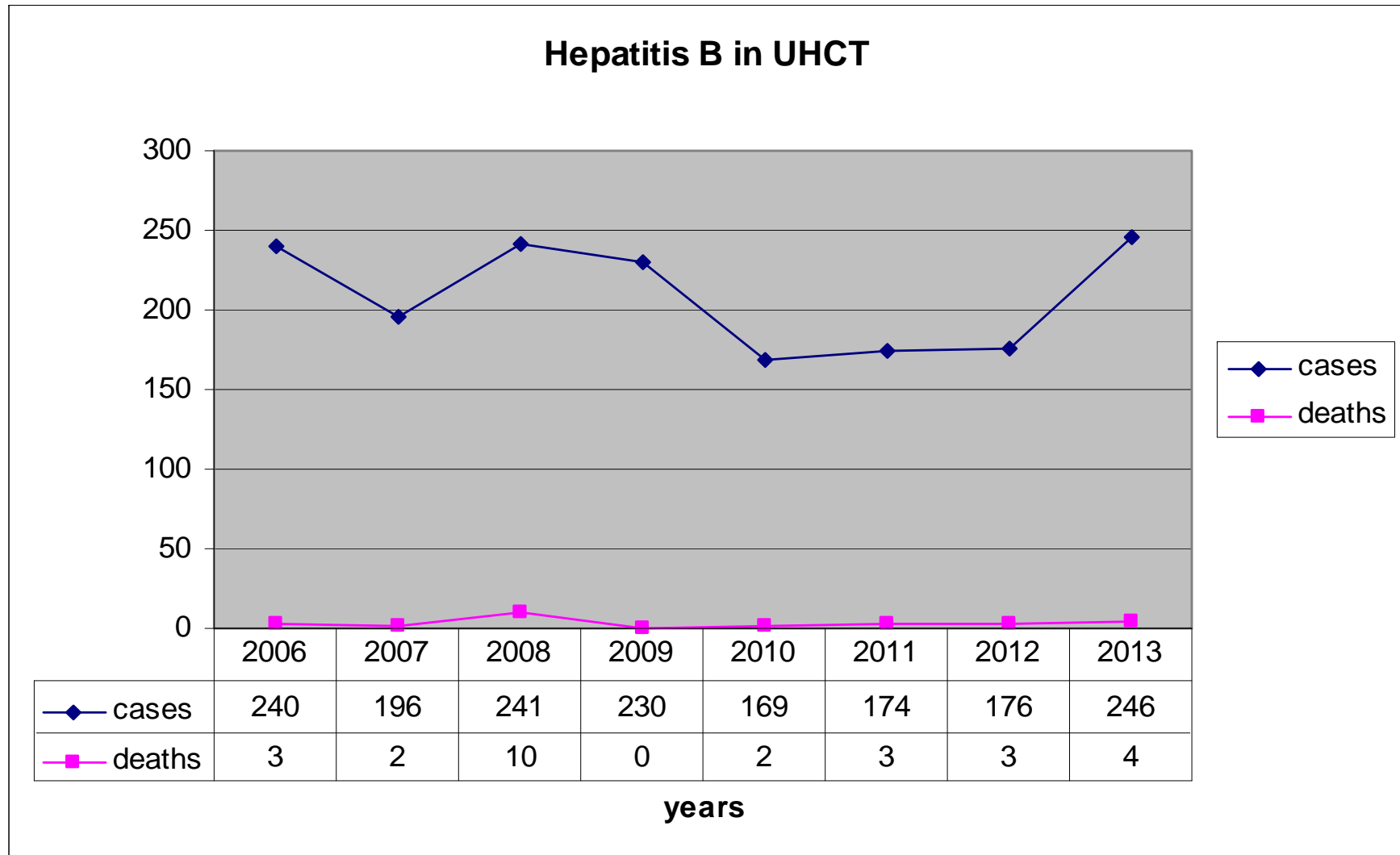
# HbsAg sero-prevalence (cross sectional sentinel study): pregnant women

- 6000 pregnant women at O-G hospital Tirana, Jan- Sept 2010.
- 15-43 yrs
- 410 HbsAg +.
- Sero-positivity rate of HBsAg among pregnant women is 6.8%

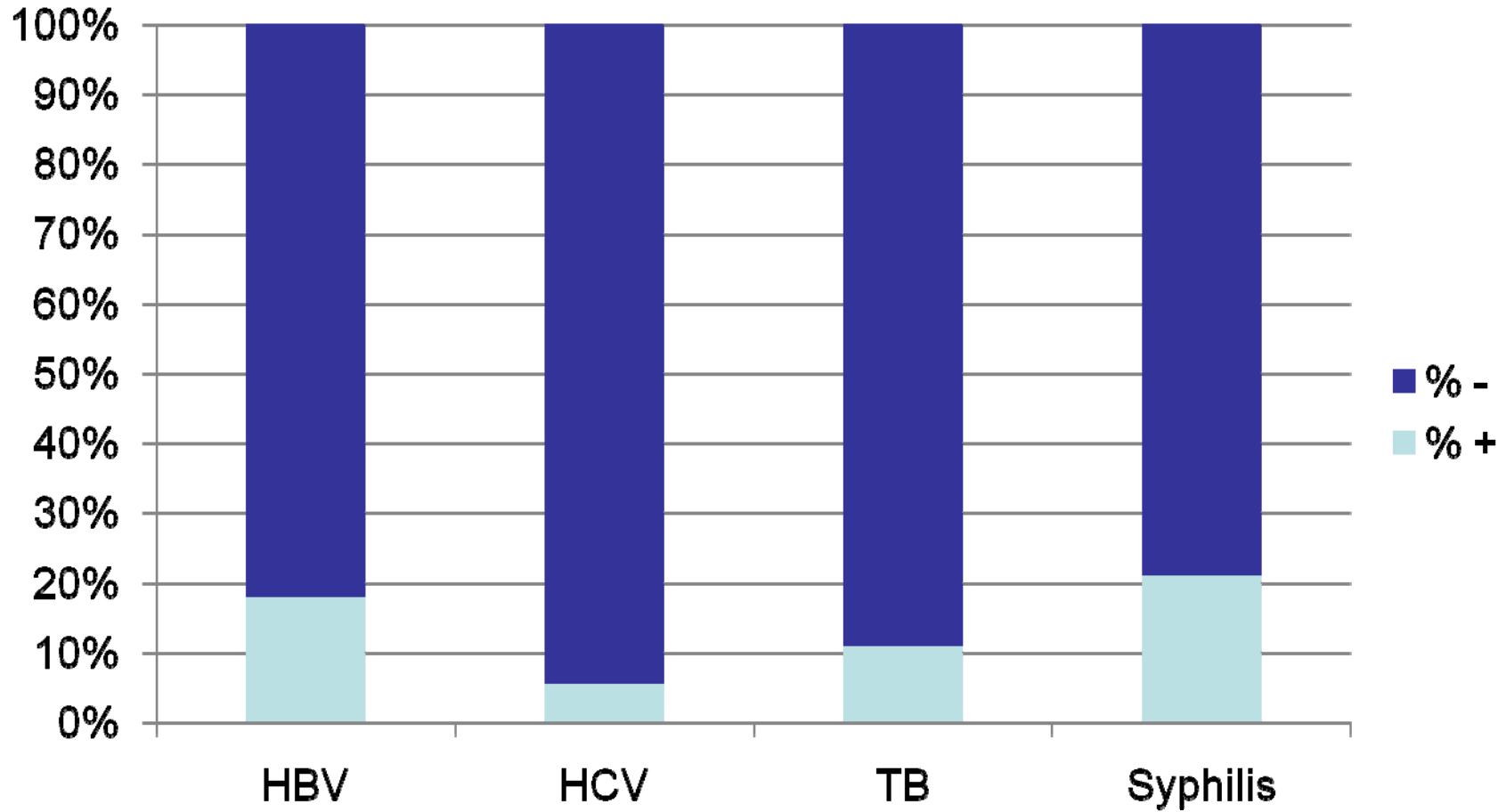
# Reported cases of Hepatitis in Albania (source IPH)



# Death rate of HBV at UHCT



# HBV (n=235), HCV (n=196) TB (n=249), sifiliz (n=194) among HIV patients





# Specialties treating CHB : GI and ID

- Infectious Disease and Gastro-hepatologist specialist at secondary (regional hospitals) and tertiary level (UHCT: ID Service and Gastro-hepatology Service)

# Infectious disease vs. Hepatologist

## **Infectious disease:**

(Historically : acute hepatitis)

- Definite acute vs. chronic is not a clear and easy task
- Different world experience: both specialties
- Antivirals (NA) were discovered and used first in HIV
- PCR technique revolutionized the ID specialty
- WHO joint program for HIV/Hepatitis and STI (hepatitis is mainly an STI)
- Common National protocols and guidelines for management of hepatitis

## **Hepatologist**

(historically chronic hepatitis)

- Historically : chronic hepatitis
- Chronic vs. end stage liver disease

# Treatment and care cascade

- Estimations of infected persons and those in need for treatment needed.
- Screening & Case detection: testing capacities especially at PHC level are weak
- ALT/AST surveillance through “population check-up” – referring for serology diagnosis
- Not all those diagnosed can enter care through so called “referral system”
- Especially vulnerable groups such as IVDU or those without health insurance do have same barriers for access to care

# EASL standards: 2012 guidelines

- Assessment of the severity of liver disease:
- Biochemical markers : ALT, AST,  $\gamma$ GT, ALP, Bil, serum albumin, globulins, CBC, PPT
- Hepatic ultrasound
- HBV DNA (real time PCR quantification assay)
- Liver necro-inflammation and fibrosis
- Monitoring of Rx: HBVDNA every 3-6 months, Hbe Ag, anti Hbe, HBs every 12 months

# Diagnostic availabilities: serology

- Serology screening & diagnosis: not full panel of sero –markers provided at public hospitals
- Quantitative HBs Ag: available only at private labs

# Diagnostic availabilities: HBV DNA

(EACL : real time PCR quantification assay; baseline, after 3 m of Rx, every 6 m)

- UHCT situation: PCR equipment available but kits are scarce and quality assurance is an issue
- HBV DNA tests provided at IPH: problems with availability of kits not covering all cases and not all the time, transporting of samples might influence the quality
- Available in private labs: cost; standardization!

# Fibroscan

- Liver stiffness measurements (Fibroscan):  
Available at UHCT since 2014
- Problems:
  - Standardization
  - Training of staff
  - Only medium size probe available

# Treatment

- HIF has included in the list of drugs these treatments
- Drugs:
  - Peg-IFN
  - NAs: LAM, TDF



# TDF: protocol of HIF

- CHB (all, including those treated with LAM resistant to treatment and cases of reactivation of infection after treatment discontinuation).
- Liver cirrhosis (compensated and decompensated ).
- HCC with HBV infection .
- Chronic carriers of HBV under chemotherapy/immunosuppressive therapy (regardless level of HBV DNA).
- Fulminant/severe HBV hepatitis.
- Infection from HBV during pregnancy .
- Co-infection HIV and HBV (together with antiretroviral therapy ).

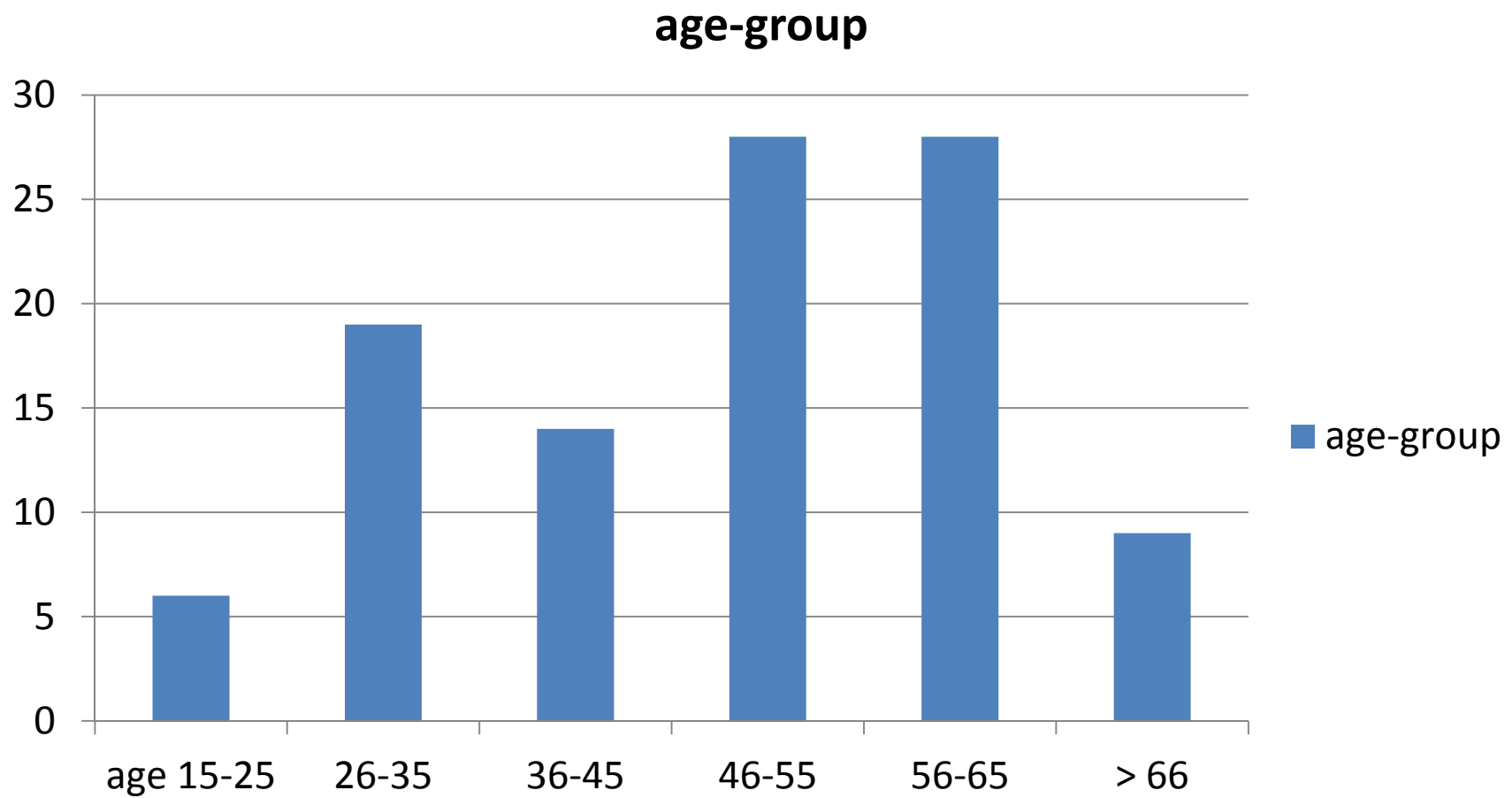
# HIF protocol: criteria

- HBV DNA > 2.000 UI/ml
- ALT > UNL
- Moderate to severe liver necro-inflammation and/or fibrosis
- (other aspects: age, health status, family history for HCC or cirrhosis, extrahepatic manifestations )
- Compensated cirrhosis: HBVDNA < 2.000 or normal ALT
- Decompensated cirrhosis: imediate treatment

# TDF use at ID Service

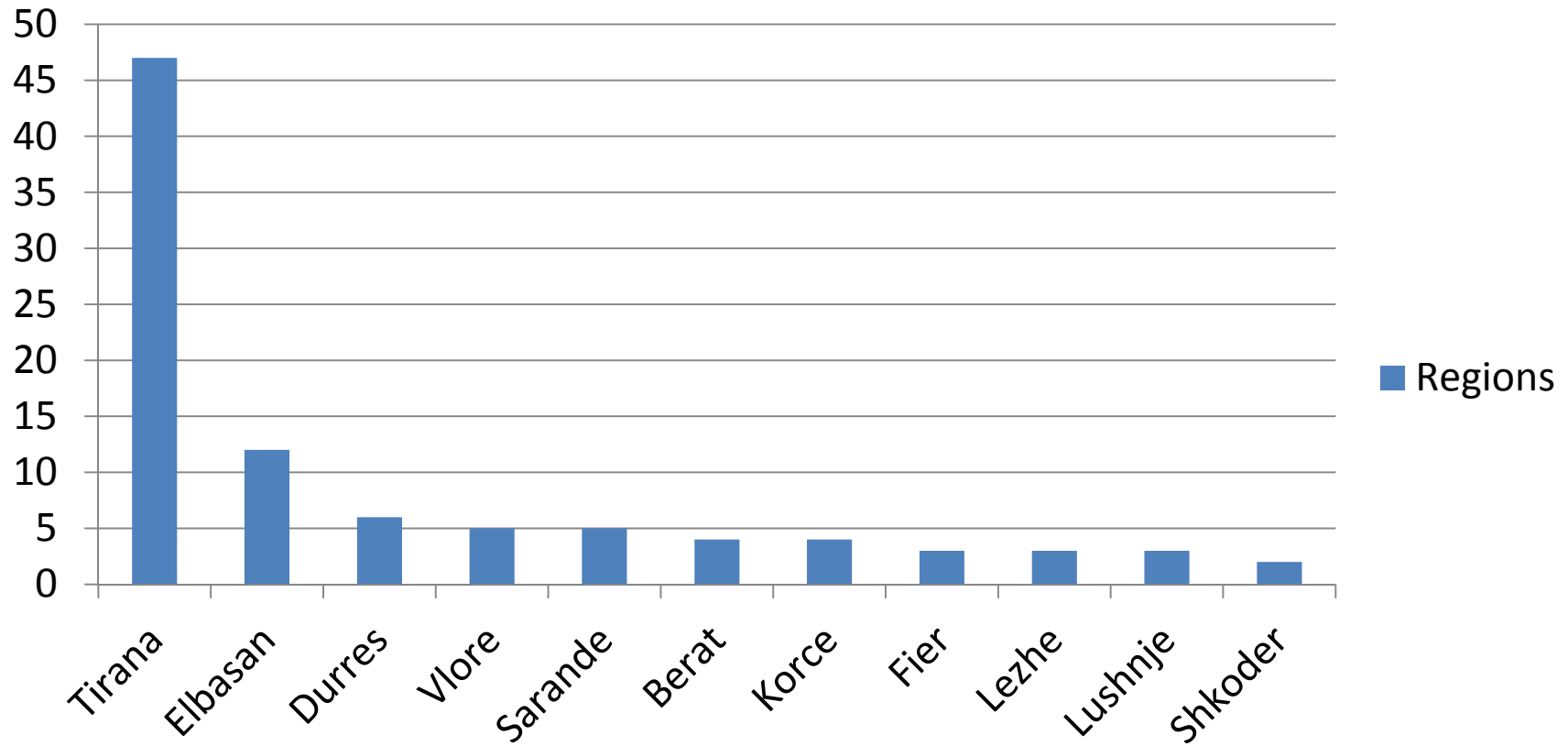
- 104 cases with HBV infection treated with TDF disoproxil at ID Service between 2014-2016
- CHB : 72 cases
- Reactivated CHB: 20 cases
- Severe acute hepatitis 12 cases

# Cases per age

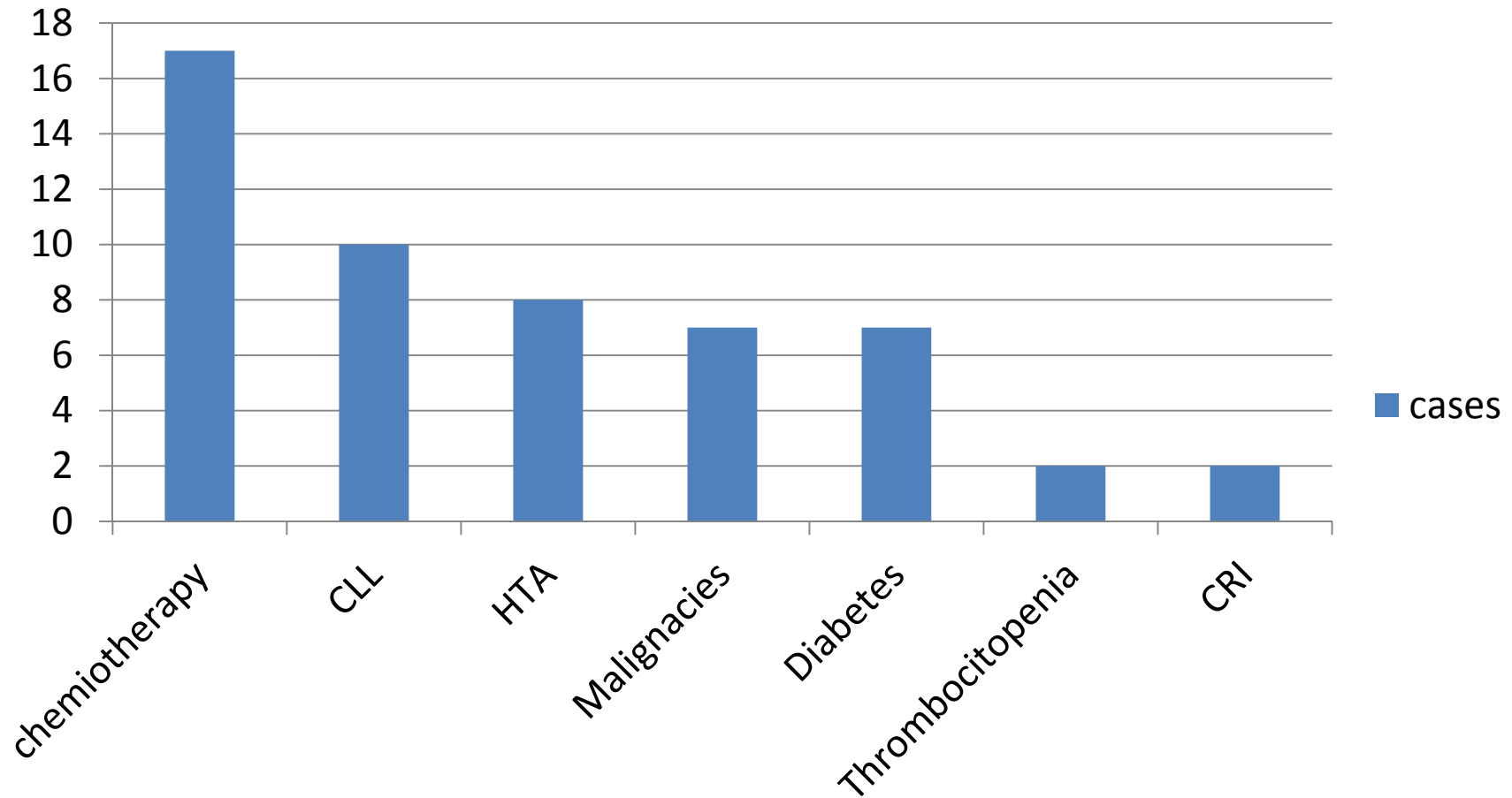


# Location

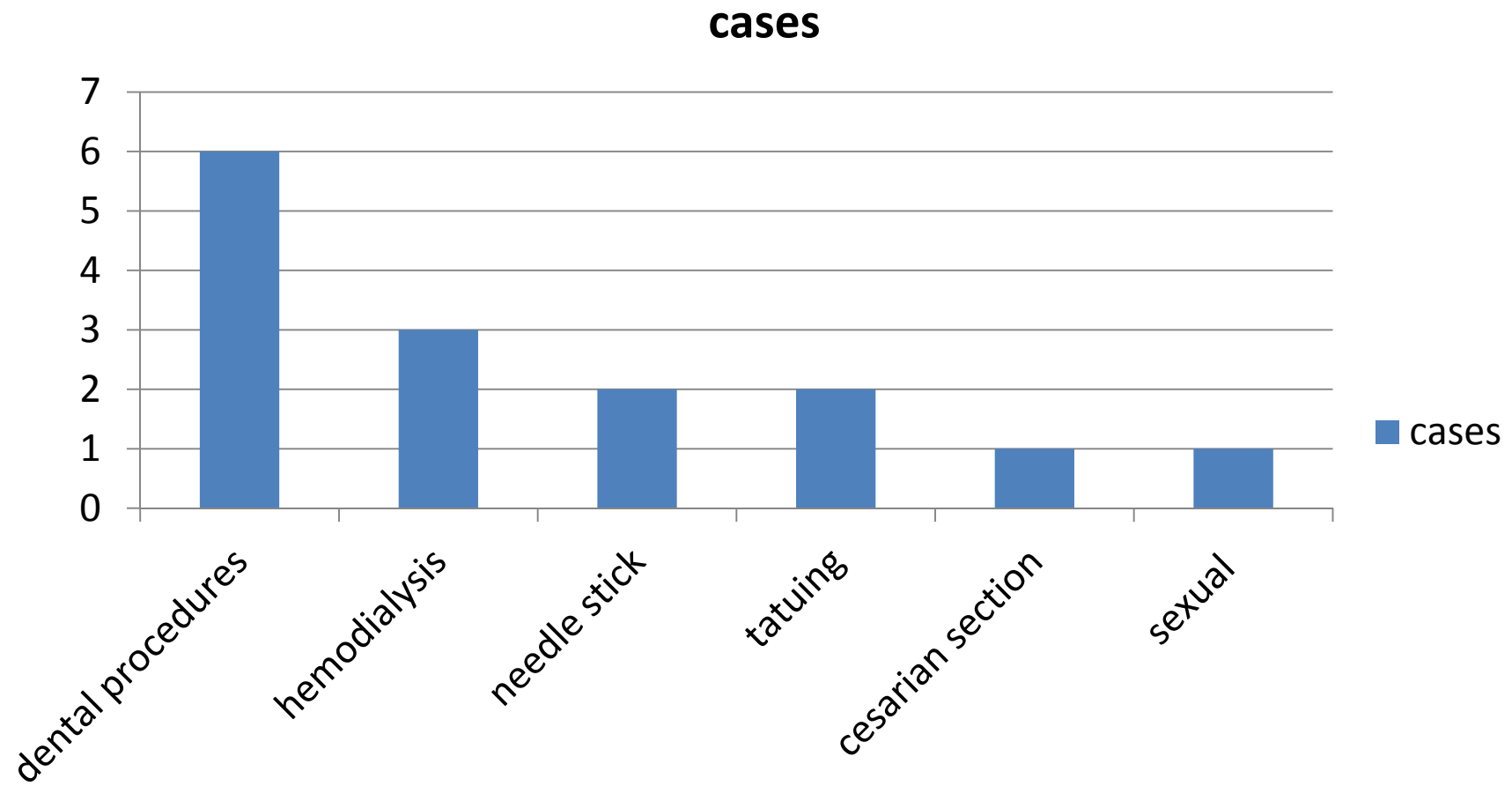
## Regions



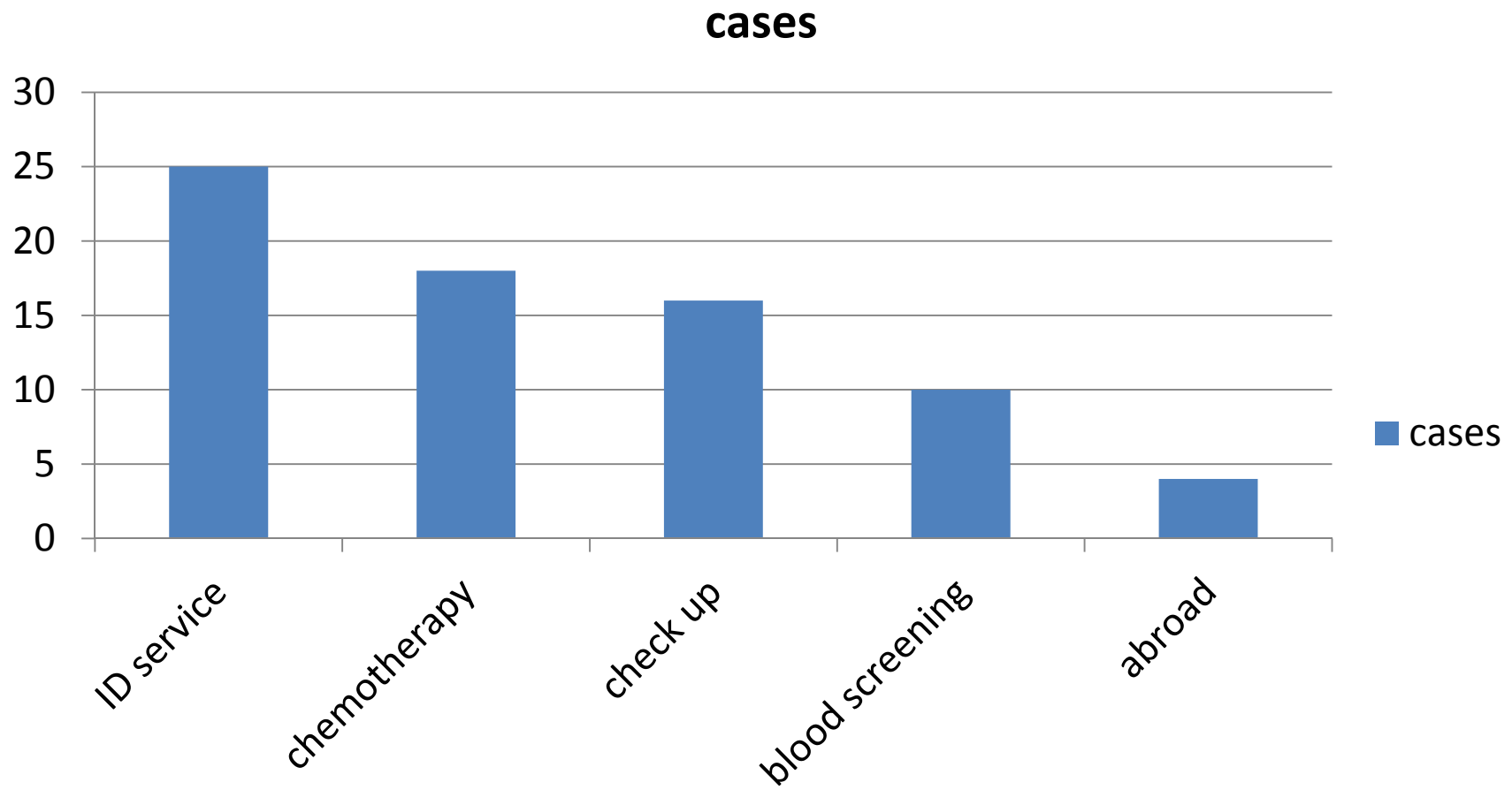
# Co-morbidities/predisposing factors



# Risk factors



# Diagnosis/testing



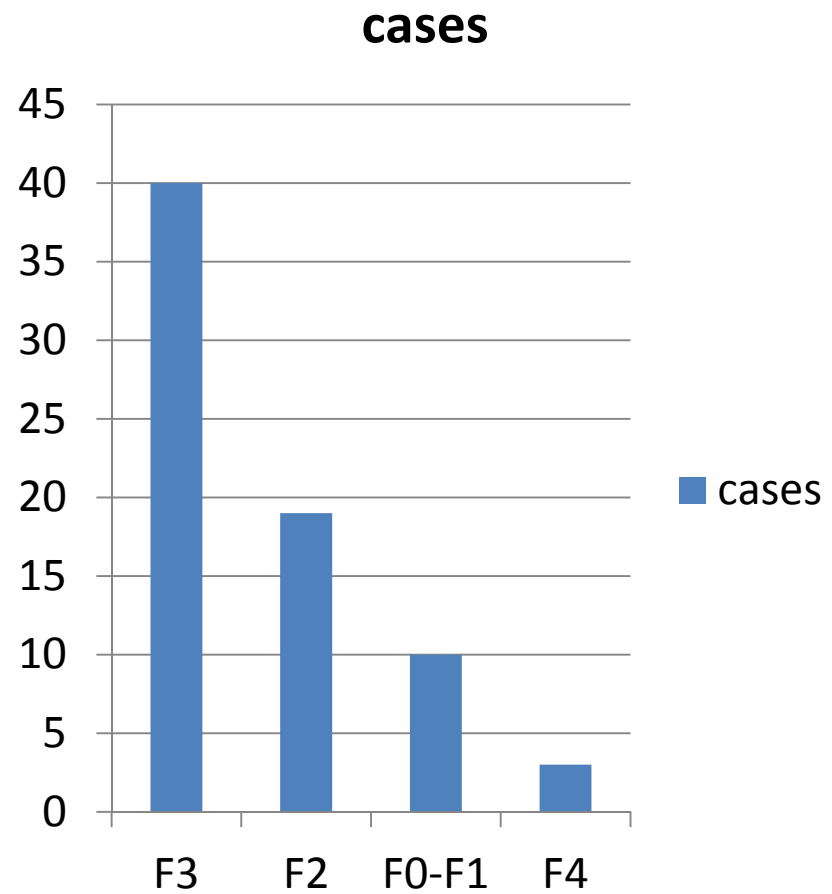


# Diagnostic criteria: ALT

- ALT: abnormal in 94 cases (out of 104)
- Median value 496 UI/L
- Range 14-2900 UI/L
- Quantitative HBs Ag measurement: 61 cases (59%) (only at baseline not follow –up)

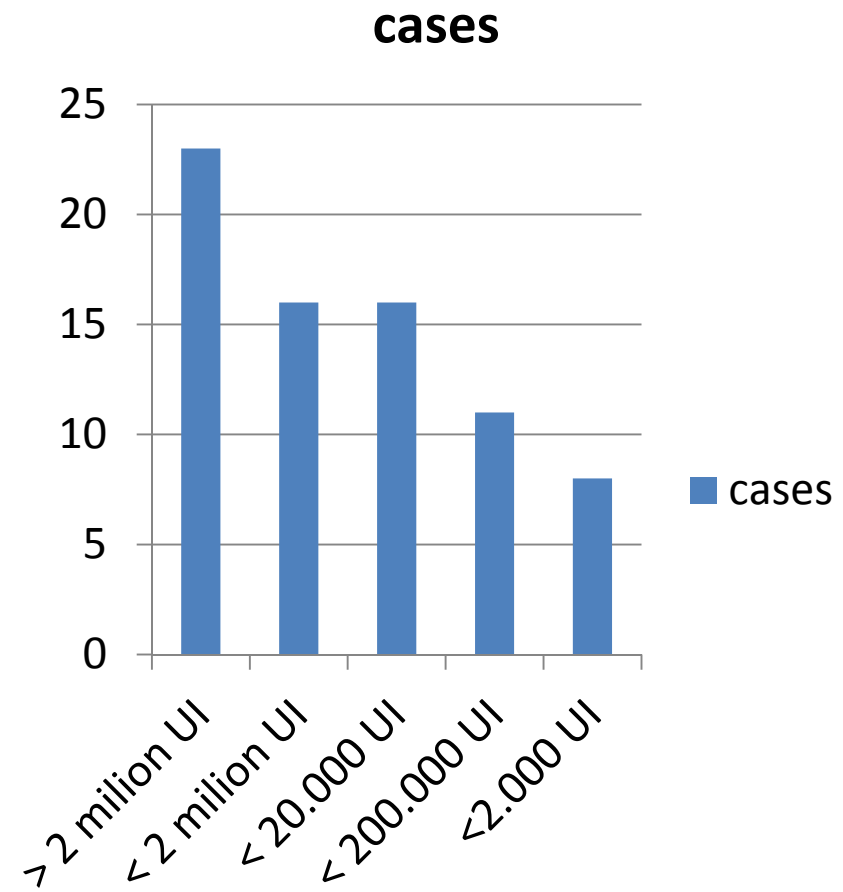
# Fibroscan

- 72 cases ( 70%)  
measurement of liver  
stiffness with fibroscan  
was performed at  
baseline



# HBV DNA

- Measured at baseline in 74 cases (72%)



# TDF in severe acute hepatitis B

- 8 cases with severe AHB at ID Service at UHCT, followed during 2013

# Characteristics

- Age: 25 yrs (21-33)
- Sex: 7/1 (F/M)
- Risk factors: dental procedures (44%), sexual (11%)
- Onset-hospitalization: 11 days (4-30 days)
- Onset-treatment: 12 days (4-33 d)

# Characteristics

- ALT: 1706 UI (1060-3300)
- **Bil : 15 mg/dl (8.4-27.2)**
- **INR: 1.94 (1.6-2.5)**
- **Encephalopathy: 12 % (1/8)**
- Hepato-splenomegaly: 75% (6/8)
- HBsAg: 100% (8/8)
- Anti HBc IgM: 100 % (8/8)
- HBeAg : 1 positive (out of 2 cases performed)
- HBV DNA : (n=2)  $3.2 \times 10^5$

# Follow up

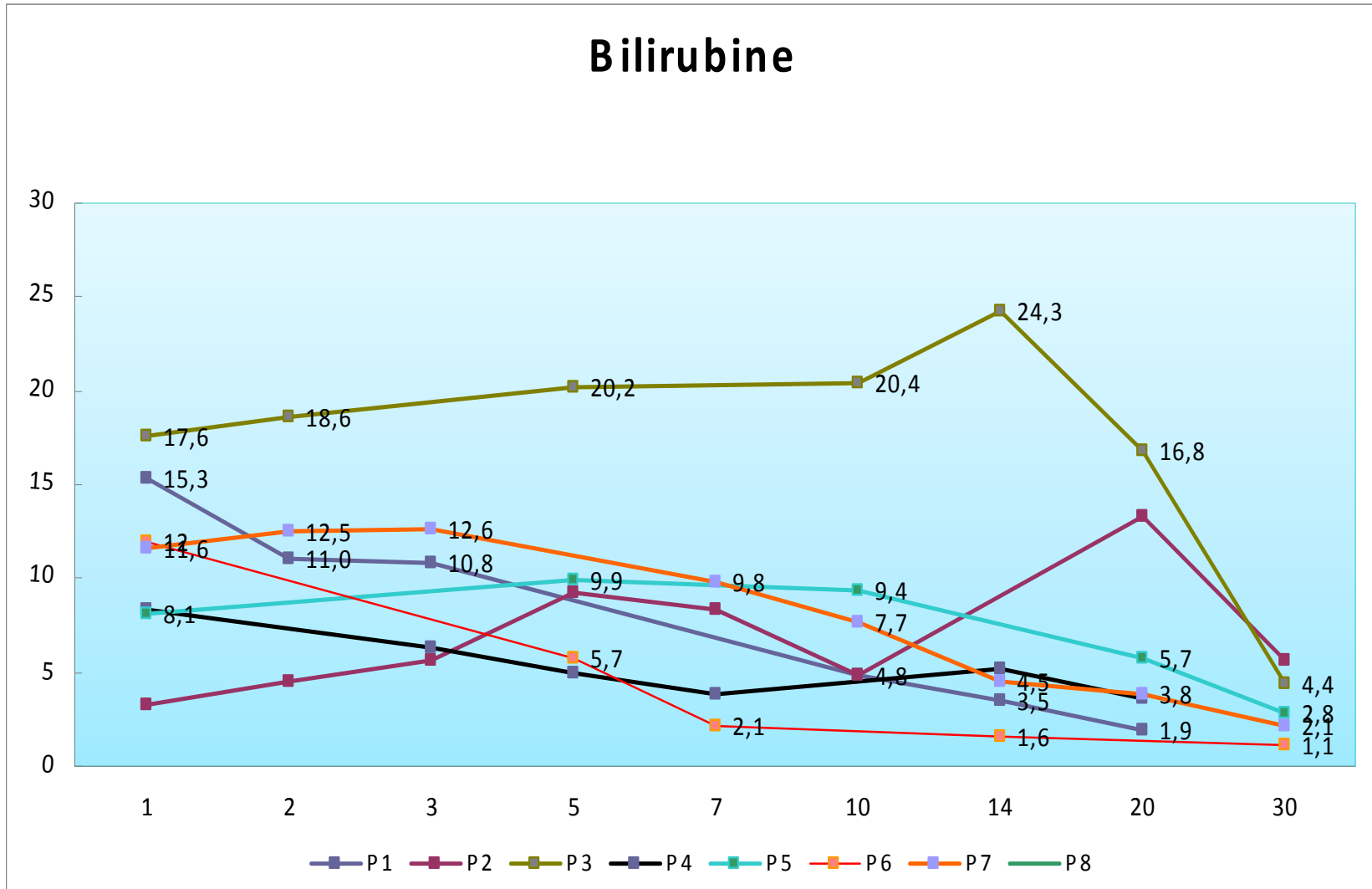
- All the patient were followed at least for 6 months ( 2 cases lost: 1 and 2 months)
- Time on treatment: 5.9 months (1-12)
- Normalization of INR: 11 days (4 days for 7 cases)
- ALT: 60 days ( n=7)
- Bil: 50 days (n=7, 26-98 d)
- All the 6 cases who were followed up became HbsAg neg, while only 2 did not seroconvert to anti Hbs Ab.
- No adverse effects to therapy

<b>Time to seroconversion and biological normalization</b>									
	<b>Patients</b>								
	1	2	3	4	5	6	7	8	<b>Mean days</b>
<b>HBV DNA</b>	NA	baseline	NA	NA	NA	NA	baseline	NA	
<b>HBsAg -</b>	180	180	180	NA	240	180	150	NA	
<b>AntiHBs</b>	180	180	180	NA	240	180	-	NA	
<b>Bilir</b>	30	65	60	-	98	30	30	40	<b>50</b>
<b>ALT</b>	30	100	60	-	98	56	60	60	<b>60</b>
<b>INR</b>	5	8	2	2	60	3	2	5	<b>11</b>
<b>TDF Rx</b>	180	180	180	30	240	180	360	60	<b>180</b>

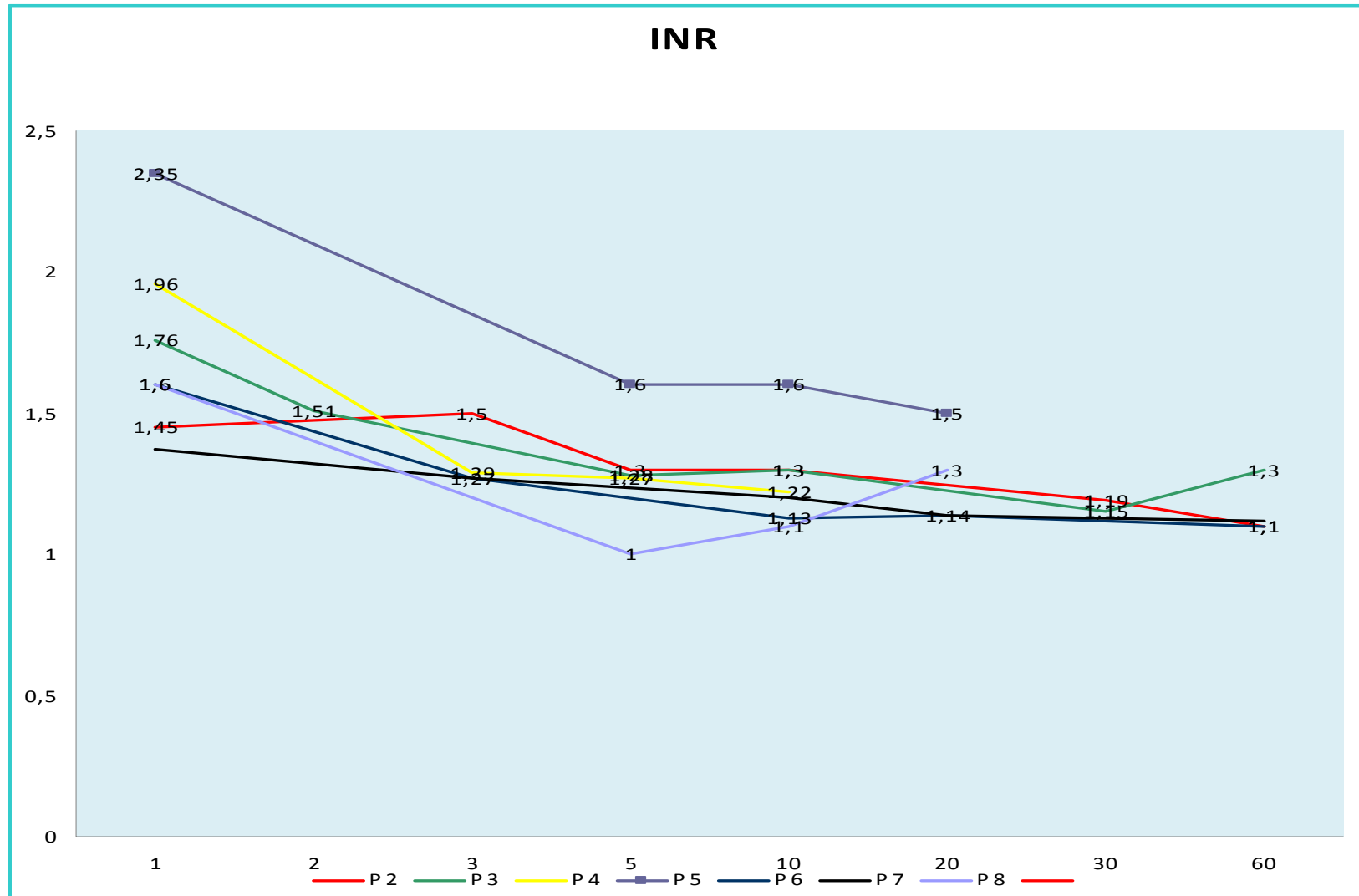




# Bilirubine



# INR



# 20 case with reactivated CHB at ID Service, UHCT

- 13 men (65%) average age 54 years.
- associated diseases :
  - Chronic lymphoid leucosis (CLL) 7 cases (35%),
  - Non Hodgkin lymphoma 5 cases (25%),
  - Hodgkin lymphoma 4 cases (20%),
  - myeloma 2 cases (10 %),
  - Breast Ca 1 case (5%)
  - Idiopathic thrombocytopenic Purpura 1 case (5%).
- Reasons of reactivation: only 3 cases serologically tested (only HBsAg) before initiation of therapy
  - 19 cases (95%) different regimens of chemotherapy
  - 1 case corticotherapy with high doses

# Clinical forms

- hepato (90%) and splenomegaly (65%),
- Icter (90%)
- bilirubinemia (medium) 7 mg/dl, range 0.3-20 mg/dl, where 8 cases (40%) had bil > 10 mg/dl,
- AST increase in 17 cases. Medium value 176 IU (7-1032),
- ALT increase in 20 cases (100%) values medium 698 UI (7-2325)
- PPT 60% (26-81%) with 1 case < 40%.
- Increase gama globulinemia in 10 cases (76%).
- 8 cases (40%) presenting severe forms.
- 18 cases (90%) treated with tenofovir disoproksil 245 mg/d PO and supportive therapy.

# Recommendations (action plan)

- Accurate estimations of sero-prevalence of HBV in Albania, especially among risk groups, estimations of those in need for treatment and care etc.
- Improve screening and diagnostics capacities at all levels of care
- Improve referral system
- Improve access and linkage to care to every one in need regardless health insurance status
- Improve treatment and care and follow up through implementation of updated national guidelines, protocols and SOP in line with WHO and other international guidelines
- Set up Hepatitis Outpatient Clinic, improve database and reporting

- Thank you!