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Jaundice in Adult in-Patients at a Tertiary General Hospital

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Abstract

Objective: The aim of the study is to investigate the "new-onset jaundice" incidence, map of causes, approaching method, and risk factors for treatment failure in adult in-patients at a tertiary general hospital as Cho Ray Hospital, Ho Chi Minh City, Viet Nam. Method: Retrospective study was done on 416 jaundice patients administered over 38 continuous days. Laboratory tests investigated were total bilirubin, direct bilirubin, AST, ALT, AST/ALT ratio, GGT, AP, bilirubin and urobilinogen in urine. Jaundice was defined as total bilirubin ≥ 2.5 mg/dL, direct bilirubin jaundice defined as direct bilirubin > 2 mg/dL and D/T percentage > 60%, the severity of AST, ALT evaluated according to Common Terminology Criteria for Adverse Events, AST/ALT ratio, and bilirubin, urobilinogen in urine. Outcome of treatment were classified in two groups: failure (dead or discharge due to worse status) and success. Descriptive statistics and analytic statistics were applied, mono-variable analysis and multinomial logistic regression to find out the independent risk factors for treatment failure. Results: The incidence of "new-onset" jaundice in adult patients was 11 ± 5 person/day. The map of jaundice included 3 phases as pre-heaptic 13.7%, in-hepatic 58.2%, and post-hepatic 22.8%. Pancreatic and biliary tract diseases accounted 17.1%, then cirrhosis 16.3%, liver tumor 14.7%, hepatitis 8.9%, sepsis 8.9%, hematology diseases 7.9%, and cardiac diseases 7.5%. A guide for approaching causes of jaundice basing on 7 parameters as total bilirubin, D/T percentage, severity of ALT, AST/ALT ratio, severity of GGT, and bilirubin and urobilinogen in urine was established. The overall mortality was 7.5% (31/416), sepsis had highest death rate of 37.8% (14/37). Sepsis and AST/ALT ratio > 2 were the two independent risk factors of mortality. Conclusion: At tertiary hospital, jaundice is common sign in adult patient, diverse enormously in many clinical wards. The map of causes of jaundice completed all 3 phases: pre-hepatic, intra-hepatic and post-hepatic phase. Drug hepatitis jaundice was an important cause in hepatitis. Sepsis had highest mortality in adult jaundice patients. Combination of 7 criteria as total bilirubin, the D/T percentage, ALT severity, AST/ALT ratio, GGT, bilirubin and urobilinogen in urine gave the guide for approaching to jaundice. Sepsis and AST/ALT ratio > 2 were independent risk factors of treatment failure. The survey of jaundice in adult in-patients in a tertiary general government hospital gave the full picture for this common pathological sign.

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Keywords

Jaundice, Adults, Incidence, Sepsis, AST/ALT Ratio, New-Onset, Tertiary Hospital

1. Introduction

Jaundice is a common sign in clinical settings, presenting as a yellowish pigmentation of the skin, the conjunctival membranes over the sclerae, and other mucous membranes caused by hyperbilirubinemia [1]. The hyperbilirubinemia is defined as the value of total bilirubin > 2.5 mg/dL [2] [3]. Jaundice in adult patients may be caused by many different diseases with severity varied from benign to life-threatening settings. Patients with jaundice in emergency room were a challenge to promptly diagnosis of the cause of jaundice as well as properly initial intervention to be made [4]. Jaundice is commonly encountered in patients in Intensive care unit, with high incidence as 40%, and high mortality [5]. In patients with trauma, the cause of jaundice was bilirubin overload due to the breakdown of transfused and extravasated blood and liver dysfunction [6]. The map of jaundice causes for adult in-patients treated in hospitals may be different from country to country. There was lack of the pre-hepatic phase causes of jaundice in 2 reports on 121 cases in South West Wales [7] and 100 cases in Stobhill Hospital, Glasgow [8] in United Kingdom. A report on 732 new-onset jaundice cases in non-referral Wishard Memorial Hospital, Indiana, USA revealed sepsis, the highest cause of jaundice 22%, and also did not remark the pre-hepatic phase causes [9]. The hematology disease was reported as 3% in 352 jaundice cases in Guangzhou Hospital, China [10]. The map of jaundice may be different between research sites due to the grade of hospital and the site of hospital.

We report the results of a retrospective study on 416 new-onset jaundice in-patients administrated over 38 consecutive days at Cho Ray Hospital, Ho Chi Minh City, Vietnam. The aims of study were to identify the incidence rate of new-onset jaundice, causes of jaundice, roles of bilirubin and liver function tests in diagnosis of jaundice, mortality and risk factors related to the treatment failure in adult jaundice in-patients.

2. Materials and Methods

2.1. Research Subjects

Cho Ray Hospital is a tertiary general government hospital, located in Ho Chi Minh City, including 43 clinical departments, 11 laboratory departments, 3 medical centers; having 1800 beds and around 2000 out-patients per day.

The study was retrospective. Data were started from the source of bilirubin results of biochemistry department. Other results of liver function test, including aspartate transaminase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (GGT), alkaline phosphatase (AP), and total urinalysis were recorded if available together with bilirubin results. The list of patients with corresponding administration was sent to the Medical Planning Room for reviewing the patient medical files to record the personal characteristics (year of birth, gender, date of administration, date of hospital discharge) and the final diagnosis and results of treatment on discharge. Hyperbilirubinemia was defined as total bilirubin ≥ 2.5 mg/dl, and classified into 3 groups, based on the percentage of direct bilirubin over total bilirubin (D/T percentage) as: <20%: increased indirect bilirubin; 20% - 60%: hepatic or post-hepatic jaundice; and >60%: post-hepatic (direct bilirubin) jaundice [11].

2.2. Statistical Analysis

Data were stored by Excel program. Statistical analysis was performed with SPSS version 18. The main statistics was descriptive with values presented as mean, median, standard deviation, range (minimum - maximum values) and percentage. Mono-variable analysis with 2 × 2 tables for relationship between risk factors with treatment outcome. Treatment outcomes were classified as 2 values: success and failure (including dead and discharge due to worse status). Multinomial logistic regression was applied to find out the independent risk factors for treatment failure. The p value < 0.05 was indicated as a significant difference.

3. Results

3.1. General Results

There were 416 jaundice cases investigated, male/female as 240/176 (57.7%/42.3%). The mean age was 53.8 ± 16.9 years old (range: 16 - 93); age distributed as <20 yrs.: 1.2%; 20 - 39 yrs.: 20.5%; 40 - 59 yrs.: 41%; ≥60 yrs.: 37%). Surgery medicine included 170 cases (41.1%), internal medicine with 246 cases (58.9%). In surgery, there were 8 departments: Liver-Biliary-Pancreas 79 cases (46.5%), Liver Tumor 43 (25.3%), Open Heart Surgery 26 (15.9%); Gastro-intestinal Surgery 8 (4.7%) and 14 cases belonging 4 others (Orthopedics, Neuro-surgery, Burn, Vascular Surgery departments). In medicine, there were 13 departments: Gastrointestinal, Liver, Biliary, Pancreatic diseases 101 cases (41.1%), Hepatitis 32 (13%), Clinical hematology 27 (11.0%), Cardiology 14 (5.7%), Palliative care 16 (6.5%), Intensive Care Unit 15 (6.1%), Tropical Diseases 13 (5.3%), Neurology 9 (3.7%) and 19 belonged to 5 (General Medicine, Pneumology, Endocrinology, Cardiac Intervention).

3.2. Causes of Jaundice

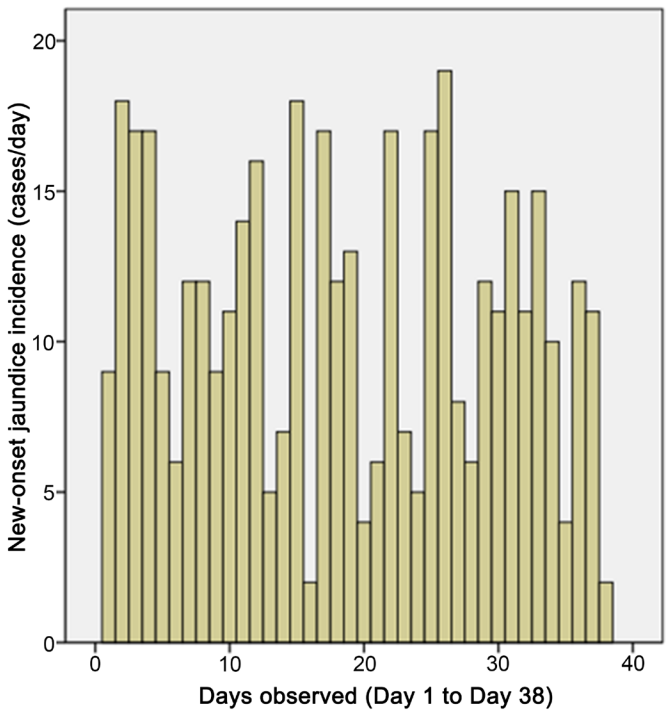
The incidence of "new-onset jaundice" in in-patients calculated over 38 consecutive days was 11 ± 5 person/day (median: 11, minimum: 2, maximum: 19) (**Figure 1**).

The causes of jaundice were presented in **Table 1**. The main diseases were pancreatic and biliary tract diseases (71, 17.1%); cirrhosis (68, 16.3%), liver tumor (61, 14.7%), sepsis (37, 8.9%), hepatitis (37, 8.9%), hematology diseases (33, 7.9%), and cardiac diseases (31, 7.5%).

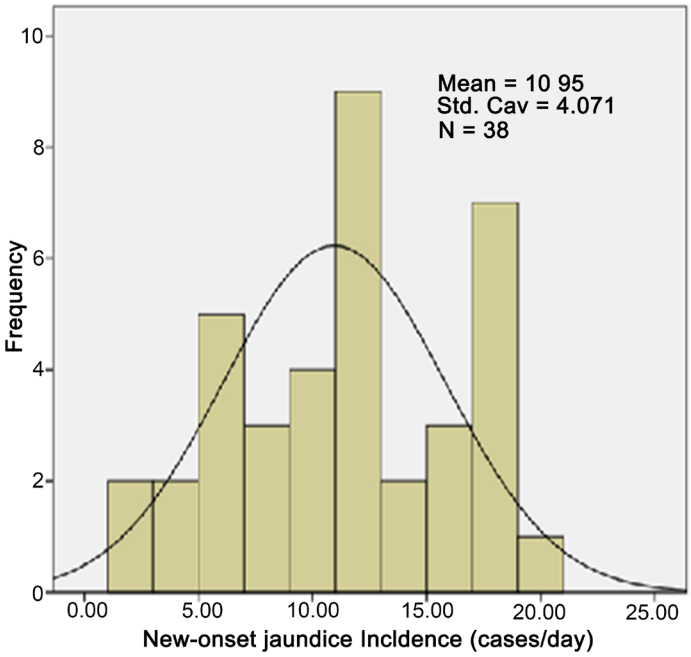
Pre-hepatic jaundice included hematology diseases, hematoma/hemorrhagy, and hemorrhagic stroke accounted 13.7% (57/416); in-hepatic jaundice (liver abscess, tumor, hepatitis, cirrhosis, trauma, sepsis, cardiac cirrhosis) 58.2% (242/416); post-hepatic jaundice (pancreatic and biliary tract diseases, cholangitis) 22.8% (95/416); and unclassified causes 5.3% (22/416).

Among 37 hepatitis cases, viral causes (hepatitis B virus, hepatitis C virus) accounted 18 cases (48.6%), drug induced liver injury 14 (DILI) (37.8%), alcoholic hepatitis 1, autoimmune diseases 1, and unclassified hepatitis 3. The total bilirubin values were high in DILI cases: 7 with >15 mg/dL, 4 with 7.1 - 15 mg/dL, and 3 with 3.1-7.0 mg/dL.

Hematoma/hemorrhagy were seen in 18 cases: multiple trauma 8 (44.4%), hemorrhagy 5 (27.8%), aortic dissection 4 (22.2%), and post-mitral valve replacement surgery.



(a)



(b)

Figure 1. Distribution of frequency of "new-onset" jaundice cases administered in Cho Ray Hospital over 38 continuous days (a). The average incidence of "new-onset" jaundice was 11 ± 5 (minimum: 2, maximum: 19) adult patients per day (mean ± SD). SD: standard deviation (b).

Table 1. Causes of jaundice in 416 patients.

Pathogen	n (%)	Pathogen	n (%)
Liver abscess	5 (1.2)	Pancreatic and biliary tract diseases	71 (17.1)
Hematology diseases	33 (7.9)	Choledocholithiasis	19
Thalassemia	9	Biliary strictures	3
Hemolysis	8	Acute pancreatitis	3
Bone marrow failure	6	Sphincter of Oddi disorder	2
Leukemia (acute, chronic)	5	Cholecystitis	1
Phagocytosis	3	Bile duct lesion	1
Multiple myeloma	1	Cholangiocarcinoma	20
Hemophilia B	1	Pancreatic cancer	10
Liver tumor	61 (14.7)	Peri-ampulary cancer	9
Hematoma/hemorrhagy	18 (4.3)	Gallbladder cancer	3
Sepsis	37 (8.9)	Hepatitis	37 (8.9)
Cholangitis	24 (5.8)	Viral hepatitis	18
Cardiac diseases	31 (7.5)	Drug induced hepatitis	14
Cirrhosis	68 (16.3)	Alcoholic hepatitis	1
Liver trauma	3 (0.7)	Autoimmune hepatitis	1
Other tumors	6 (1.4)	Unclassified hepatitis	3
Hemorrhagic stroke	6 (1.4)	Other	28 (5.0)

3.3. Characteristics of Bilirubin and Other Liver Function Tests in Jaundice Patients

The characteristics of bilirubin were presented in **Table 2**. There were 182 cases (43.7%) with total bilirubin ≥ 6 mg/dl (CTC grade III); 76.2% with D/T percentage > 60%, and 49.3% with bilirubin positive in urine.

In hepatitis ALT increased >5 times over UNL (upper normal limit) accounting 59.5% (22/37). In cirrhosis, there were 22/68 cases (32.4%) having normal or low ALT. Hematology disease with jaundice often had ALT in normal range 51.5% (17/33) (**Table 3**).

AST/ALT ratio ≥ 2 was seen mainly in cirrhosis (52/68: 76.5%), liver tumors (36/61: 59%), hematoma/hemorrhagy (11/18: 61.1%), sepsis (18/37: 48.6%). Inversely, in hepatitis AST/ALT ratio was <1 (16/37: 43.2%) (**Table 4**).

Table 2. Characteristics of bilirubin in 416 cases.

Parameters	Results		Parameters	Results	
Total bilirubin (mg/dL)	8.1 ± 7.1 5.2 (2.5 - 42.2)		Direct bilirubin (mg/dL)	6.0 ± 5.9 3.6 (0.4 - 32.4)	
Distribution of total bilirubin (mg/dL)			D/T percentage (direct Bilirubin/total bilirubin) (%)		
≥2.5 - <3.0	69	16.6%	≤20%	19	4.6%
≥3.0 - <6.0	165	39.7%	>20% - ≤40%	26	6.3%
≥6.0 - <15.0	124	29.8%	>40% - ≤60%	54	13%
≥15.0	58	13.9%	>60%	317	76.2%
Bilirubin in urine (n = 136)			Urobilinogen in urine (mg/dL) (n = 136)		
Negative	69	50.7%	0.1	81	59.5%
+	17	12.5%	1	22	16.2%
++	13	9.6%	4	14	10.3%
+++	37	27.2%	8	19	14.0%

Table 3. Distribution of ALT in relating diseases in 413 jaundice cases.

Pathogen	Level of ALT (compared to upper normal limit 35 U/L)					Total
	≤1	>1 - 2.5	>2.5 - 5	>5 - 20	>20	
Liver abscess	1	2	2	0	0	5
Liver trauma	0	2	0	1	0	3
Hematology diseases	17	6	7	2	1	33
Liver tumors	16	21	7	17	0	61
Other tumors	1	2	2	1	0	6
Hematoma/hemorrhages	7	5	1	3	2	18
Pancreatic and biliary tract diseases	4	29	19	17	1	70
Sepsis	7	17	7	6	2	37
Cholangitis	3	11	8	1	0	23
Cardiac diseases	11	6	3	6	5	31
Hepatitis	3	8	4	11	11	37
Hemorrhagic stroke	1	2	0	1	2	6
Cirrhosis	22	30	10	6	0	68
Other	4	5	3	2	1	15
Total	97	144	73	74	25	413

Table 4. AST/ALT ratio and pathological causes of jaundice (n = 412).

Pathogen	AST/ALT ratio			Total
	<1	≥1 - <2	≥2	
Liver abscess	1	3	1	5
Liver trauma	0	2	1	3
Hematology diseases	6	12	15	33
Liver tumors	7	18	36	61
Other tumors	3	2	1	6
Hematoma/hemorrhage	1	6	11	18
Pancreatic and biliary tract diseases	17	40	13	70
Sepsis	2	17	18	37
Other	2	5	8	15
Cholangitis	6	8	9	23
Cardiac diseases	7	11	13	31
Hepatitis	16	12	9	37
Hemorrhagic stroke	2	2	2	6
Cirrhosis	3	13	52	68
Total	73	151	189	412

The total bilirubin values were divided into 2 groups: total bilirubin > 7 mg/dL were seen in pancreatic and biliary tract diseases (47/72: 65.3%), hepatitis (23/37: 62.2%), cholangitis (13/24: 54.2%), and another group with total bilirubin ≤ 7 mg/dL including hematology diseases (27/33: 81.8%), liver tumor (46/61: 75.4%), hematoma/hemorrhagy (16/18: 88.9%), sepsis (26/37: 70.3%), cardiac diseases (25/31: 80.6%) and cirrhosis (42/68: 61.8%).

The direct bilirubin increased, with D/T percentage > 60%, were seen in hepatitis 100% (37/37), sepsis 97.3% (36/37), cholangitis 95.8% (23/24), pancreatic and biliary diseases 95.8% (69/72), liver tumor 77.4% (48/62), cirrhosis 60.3 (41/68). Inversely, the pathologies without increase direct bilirubin (D/T < 60%) were hematology disease 63.6% (21/33), cardiac disease 54.8% (17/31), hematomas/hemorrhagy 50% (9/18). Especially, the D/T percentage ≤ 20% presented mainly in hematology diseases 57.9% (11/19). There were 3 cases diagnosed as congenital non-hemolytic, increased indirect bilirubinemia (3/416, 0.7%).

In 71 patients with obstructive biliary jaundice, 69.2 patients (27/39 cases) had Gamma-glutamyl transferase (GGT) grade CTC2 (>2.5 UNL, UNL = 38 U/L), and 50% (12/24 cases) had Alkaline phosphatase (AP) grade CTC2 (>2.5 UNL, UNL = 148 U/L).

Table 5 presented the combination of 7 parameters including total bilirubin, D/T percentage, the severity of ALT compared to the UNL of 35 U/L, AST/ALT ratio, bilirubin in urine, urobilinogen, and the severity of GGT compared to the UNL of 38 U/L in the common causes of jaundice in adult patients.

3.4. Treatment Results in Jaundice Patients

The percentage of successful treatment in jaundice patients was 92.5% (385/416). Sepsis was the cause with highest treatment failure as 37.8% (14/37). The failure rates were lower in cardiac diseases (9.7%, 3/31), cholangitis (8.3% 2/24), hematology diseases (6.1%, 2/33), and cirrhosis (4.4%, 3/68) (**Table 6**). In hepatitis, 1 case died due to acute hepatitis after using antithyroid drugs (1/14:7.1%).

Table 7 showed there were 2 risk factors for treatment result including sepsis and AST/ALT ratio ≥2 with failure rates as 37.8% (14/37) and 11.6% (22/189), respectively. Multinomial logistic regression analysis confirmed that the two above factors were independent in effect to the treatment failure rate in jaundice patients (**Table 8**).

Table 5. Summary of biochemistry characteristics between causes of jaundice.

	Total bilirubin (mg/dL)	D/T*(%)	Severity ALT (35 U/L)	AST/ALT ratio	Bili/urine	Urobilinogen/urine	Severity GGT (38 U/L)
Hematology diseases	≤7	≤20	≤1	≥2	−	Normal/increase	≤1
Hematoma/hemorrhagy	≤7	≤60	≤2.5	≥2	−	Normal/increase	≤2.5
Cardiac diseases	≤7	≤60	≤2.5	1 - 2	−/+	Normal/increase	≤2.5
Sepsis	≤7	>60	≤2.5	≥2	−	Normal	>5
Cirrhosis	≤7	>60	≤2.5	≥2	−/+	Normal/increase	≤5
Liver tumor	≤7	>60	≤2.5	≥2	−/+	Normal/increase	≤5
Pancreatic and biliary tract diseases	>7	>60	≤5.0	1 - 2	+++	Normal	>5
Cholangitis	>7	>60	≤5.0	1 - 2	++	Normal	>5
Hepatitis	>7	>60	>5	<1	++	Normal	≤5

*D/T: direct bilirubin/total bilirubin (%).

Table 6. Treatment results of 416 jaundice patients.

Clinical diagnosis	Patient status on hospital discharge			Total
	Failure		Success	
	Dead	Worse illness discharging	Good progress	
Liver abscess	0	0	5	5
Liver trauma	0	0	3	3
Hematology diseases	2	0	31	33
Liver cancer	0	2	59	61
Other cancer	0	0	6	6
Hematomas/hemorrhage	0	1	17	18
Pancreatic and biliary tract diseases	1	0	70	71
Sepsis	11	3	23	37
Cholangitis	2	0	22	24
Cardiac diseases	3	0	28	31
Hepatitis	1	0	36	37
Hemorrhagic stroke	0	0	6	6
Cirrhosis	3	0	65	68
Other	1	1	14	16
Total	24	7	385	416

Table 7. Mono-variable analysis of 8 risk factors against treatment failure in jaundice patients.

Factors	Values	Treatment results		p	Factors	Values	Treatment results		p
		Failure	Success				Failure	Success	
Pathogens	Sepsis	14	23	0.000*	AST/ALT ratio	<2	9	215	0.003*
	Other	17	362			≥2	22	167	
Total bilirubin (mg/dL)	≤7	18	242	0.74	GGT (38 U/L)	≤5 UNL	1	16	0.8
	>7	13	143			>5 UNL	2	20	
D/T percentage (%)	≤60	4	95	0.21	Bilirubin in urine	−/+	6	80	1.0
	>60	27	290			++/+++	3	47	
ALT (35 U/L)	≤5 UNL	21	293	0.36	Urobilinogen in urine	normal	7	96	0.9
	>5 UNL	10	89			increased	2	31	

*Significant difference; UNL: upper normal limit.

Table 8. Multinomial logistic regression on independent risk factors for treatment failure in jaundice patients.

Factors	Value	Failure (%)	Mono-variable analysis			Multinomial analysis		
			p	OR	95% KTC	p	OR	95% CI
Pathogen	Sepsis	37.8	0.001*	12.9	5.7 - 29.5	0.000*	14.04	5.9 - 33.3
	Other	4.5						
AST/ALT ratio	≥2	11.6	0.003*	3.1	1.4 - 7.0	0.004*	3.5	1.5 - 8.4
	<2	4.0						

*Significant difference; CI: confidence interval.

4. Discussion

The mean age of jaundice patients was 53.8 ± 16.9 years old, similar to study on 352 Chinese cases, 54.4 ± 16.0 yrs [10], and 66 (1 - 93) yrs on 121 British cases [7], so old age is predominant in adult jaundice patients. Males were more predominant than females with ratio as 1.4 in this study population, similar to that from study of Whitehead NW 2001 (ratio 1.47) [7], and lower than that of Yu Z, 2012 (ratio 1.9) [10].

The important point of this study was the incidence of "new-onset jaundice" in in-patients. The incidence rate of 11 ± 5 new-onset jaundice cases per day at Cho Ray Hospital was a highest rate, compared to 121 jaundice cases detected over 7 months at 2 hospitals in South West Wale, British [7], 352 cases over 2 years (2004-2006) at Sun Yat-Sen Memorial Hospital, Guangzhou, China [10], and 732 cases over 5 years (1999-2003) at Wishard Memorial Hospital, Indiana, USA [9]. The main causes for the difference in incidence rate or load volume of adult jaundice patients could be due to the tertiary level of general hospital of Cho Ray Hospital and the hospital is the referral center for all provincial hospitals in the South of Viet Nam including hospitals in Ho Chi Minh City (with population of around ten millions of peoples). The number of 416 "new-onset jaundice" cases over 38 days showed that jaundice patients accounted an important volume in the total in-patient population in Cho Ray Hospital and the properly approach to diagnosis and management is required [7].

The location of jaundice patients by hospital specialty divided 2 parts: surgery accounted for 41.1% and internal medicine 58.9%. There were 170 patients located in 8 departments of surgery and 246 patients in 13 departments of internal medicine. These parameters showed the enormously distribution of jaundice patients in a big hospital at tertiary level as Cho Ray Hospital. In study of Whitehead MW 2008, 121 jaundice patients distributed in 5 departments of internal medicine and one of surgery, surgery accounted for 21% of total jaundice patients [7].

The map of causes of jaundice was presented in **Table 1**. There was a long list of causes of jaundice. Pancreatic and biliary tract diseases were the major cause accounted 17.1%, then cirrhosis 16.3%, liver tumor 14.7%, hepatitis 8.9%, sepsis 8.9%, hematology diseases 7.9%, and cardiac diseases 7.5%. The main causes of jaundice on 121 British cases in study of Whitehead MW were malignancy 34.7%, sepsis 22.3%, cirrhosis 20.7% were. However, in 100 British jaundice cases investigated at Stobhill Hospital, Glasgow in study of Forrest EH, 2002 showed other trend of causes of jaundice in which alcoholic liver disease (ALD) was the predominant cause, then gall-stone, malignancy. The investigation on 732 new-onset jaundice cases at Wishard Memorial Hospital, Indiana, USA showed sepsis the highest incidence of jaundice, 22% [9]. It seems that the feature of jaundice map are different between study sites. In the developed countries sepsis is predominant cause of jaundice. However, all of three studies in developed countries did not mention about the causes of pre-hepatic jaundice. At Cho Ray Hospital, we recorded causes of all 3 phases of jaundice including pre-hepatic jaundice accounted 13.7%, in-hepatic 58.2%, and post-hepatic 22.8%. So, the map of causes of jaundice in adult in-patients at Cho Ray Hospital was completed.

Pre-hepatic causes were recorded as 3% in 352 cases at Sun Yat-Sen Memorial Hospital, Guangzhou, China [10]. Hemolysis, thalassemia, bone marrow failure, leukemia, hematomas, severe hemorrhagy were the main causes of pre-hepatic jaundice in our study. It is because that Cho Ray Hospital has a clinical hematology department for blood diseases and a Trauma and Orthopedic department to receive many trauma cases. There were 3 cases diagnosed as congenital non-hemolytic, increased indirect bilirubinemia (3/416, 0.7%), suggesting the presence of Gilbert Syndrome. Yu Z 2012 reported this clinical disease about 0.85% in Chinese jaundice patients [10].

We had 37 hepatitis cases in which viral causes accounted 18 (48.6%) and drug induced liver injury (DILI) 14

(37.8%). This showed that DILI was an important cause of hepatitis now in the recent decades when treatment by drugs is going to be increased. There were 7 drug jaundice cases compared to 2 viral hepatitis jaundices in 121 cases in study of Whitehead MW, 2001 [7]. Drug hepatitis accounted as 32% in 93 hepatitis jaundice cases in study of Yu Z 2012 [10]. DILI was accounted as 4% compared to viral hepatitis 9% in 732 jaundice cases at Wishard Memorial Hospital, Indiana, USA [9]. Thus, drug hepatitis is the important cause paid attention when assessing the causes of hepatitis. The total bilirubin values were high in 14 DILI cases in our study: 7 with > 15 mg/dL, 4 with 7.1 - 15 mg/dL, and 3 with 3.1 - 7.0 mg/dL, fitting to the Hy'law for diagnosis of acute hepatitis due to drug according to the guidance of U.S. Department of Health and Human Services, 2009 [12].

There were 71 cases with obstructive jaundice divided as malignant causes (43, 60.6%) including cholangiocarcinoma, pancreas cancer, peri-ampulary cancer and gallbladder cancer; and benign causes of 39.4% in which choledocholithiasis was the main cause (**Table 1**). Malignant causes accounted 58.6% of 116 obstructive jaundice cases in study of Chalya 2011 in northwestern Tanzania [19] and 56.7% in 60 cases in Pakistan [13].

Liver enzyme as ALT was revealed as normal to <2.5 UNL (CTC1) in cirrhosis, hematology diseases and cardiac liver diseases, but was >5 UNL (CTC3) in hepatitis according to CTCAE, 2010 [14]. Thus, ALT values showed the status of liver necrosis in different causes of jaundice. The AST/ALT ratio was ≥2 occupied 76.5% in 68 cirrhosis patients, inversely this ratio < 2 was seen in 75.7% in 37 hepatitis patients. Combining these 2 parameters, ALT and AST/ALT ratio, helped to identify the levels of hepatocellular damages as well as hepatic failure in hepatitis or cirrhosis.

The total bilirubin could be divided into 2 grades by cut-point of 7 mg/dL. Hepatitis and obstructive biliary jaundice often had total bilirubin > 7 mg/dL, inversely jaundice due to other causes as hematology diseases, cirrhosis, liver tumor, sepsis, cardiac cirrhosis had total bilirubin < 7 mg/dL. Hemolysis alone rarely produce total bilirubin > 4 mg/dL, but extra-hepatic obstruction or hepatitis can cause the increase bilirubin up to 2 mg/day [15].

Increase direct bilirubin with D/T percentage > 60% were recorded as high as 100% in jaundice patients with hepatitis, pancreatic and biliary tract diseases, sepsis, cholangitis. The values of D/T percentage used for diagnosis as increase direct bilirubinemia were changed from 50%, 60% or 70% by different experts [11] [16]-[18]. The high percentages of increase GGT grade CTC2 and AP Grade CTC 2 as 69.2% and 50%, respectively, showed that combination of these 4 parameters, direct bilirubin, D/T percentage, GGT and AP, with the absence of urobilinogen in urine were the good indicators for diagnosis of obstructive biliary diseases in jaundice patients. There were only 136 jaundice patients having urine test, 32.7%, meaning that physicians, in routine clinical practice, did not pay attention to the great value of urine analysis in diagnosis of causes of jaundice. **Table 5** gave the summary of biochemistry characteristics between causes of jaundice. The combination of 7 characteristics including total bilirubin, D/T percentage, ALT level, AST/ALT ratio, bilirubin in urine, urobilinogen in urine, and GGT level could give a guide towards the causes of jaundice.

Table 6 presented the treatment result of 416 jaundice cases with general mortality as 7.5% (31/416). Sepsis was the jaundice cause with highest treatment failure as 37.8% (14/37). The failure rates were lower in cardiac diseases (9.7%, 3/31), cholangitis (8.3% 2/24), hematology diseases (6.1%, 2/33), and cirrhosis (4.4%, 3/68). Overall mortality in 121 jaundice patients in South West Wales was 31%, higher than that from our study (7.5%). The greatest mortality was recorded highly in sepsis/shock as 51%, then lower as 24% in malignant diseases and 23% in cirrhosis [7]. Chalya PL, 2011 reported the mortality rate was 15.5% in obstructive biliary jaundice patients, but higher as 33% if having postoperative sepsis [19]. Serum bilirubin levels on Intensive Care Unit admission were associated with ARDS development and mortality in sepsis. For each 1.0 mg/dL increase in admission bilirubin, ARDS risk, 28- and 60-day ARDS mortalities were increased by 7%, 20%, and 18%, respectively in study on 326 septic patients [20]. All results of these jaundice studies and that from our study showed that sepsis was the main cause of death in jaundice patients. This finding will help physicians to pay more attention of stratification of jaundice patients as well as in giving properly treatments.

In 14 drug hepatitis cases, 1 case died due to acute drug hepatitis after using antithyroid drugs (1/14:7.1%). This result was as the same as those reported in other studies, as 0% mortality among 29 patients with DILI [9] and 0% mortality in 7 drug jaundice patients in study of Whitehead 2001 [7].

Mono-variable analysis of 8 risk factors against treatment failure in jaundice patients showed in **Table 7**. There were only 2 factors having the significant relation to treatment failure in jaundice patients including sepsis and AST/ALT ratio > 2. The multinomial regression analysis confirmed again that these 2 factors were still independent risk factors for treatment failure in jaundice patients.

5. Conclusion

In conclusion, jaundice is a common sign in adult in-patients administered at the tertiary Cho Ray Hospital with the new-onset incidence rate as 11 ± 5 person per day. Jaundice patients distributed enormously in 21 diverse clinical departments. The map of causes of jaundice was completed with all 3 phases: pre-hepatic 13.7%, intra-hepatic 58.2%, and post-hepatic 22.8%. In hepatitis jaundice, drug induced liver injury (DILI) occupied as an important cause. Sepsis was the important cause of dead in adult jaundice patients. Approaching adult jaundice patients by 7 criteria as total bilirubin, the D/T percentage, ALT severity, AST/ALT ratio, GGT, bilirubin and urobilinogen in urine gave the guide for diagnosis of causes of jaundice. Finally, the independent risk factors of treatment failure in adult jaundice patients were sepsis and AST/ALT ratio > 2. The survey of jaundice in adult in-patients in a tertiary general government hospital gave the full picture for this common pathological sign.

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