A Pilot Study to Assess Transfusion Transmission of Hepatitis C Virus

Ahmed El-Nawawy¹ · Shams Abdel-Fattah Arafa² · Adham Ahmed Badeib¹ · Manal A.-M. Antonios¹

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Abstract Alexandria University blood bank adopted double screening tests: a fully automated chemiluminescence immunoassay followed by nucleic acid testing. The aim of the study was to assess the efficiency of dual check of HCV in preventing transfusion related infection among patients admitted to PICU. A prospective cohort study was carried on patients admitted to PICU during 6 months. The included patients performed HCV RNA detection on admission by conventional reverse transcriptase polymerase chain reaction (RT-PCR) technique. Only negative cases were recruited, then patients receiving blood or its product were checked after 4 weeks from discharge by RT-PCR for HCV RNA. A total of 33 patients received 108 transfusions: 9 patients of them deceased during PICU stay and the remaining 24 patients were all found to be negative for HCV. The dual screening of HCV should be implemented in all blood banks of Egypt especially for critically ill pediatric patients.

Keywords Hepatitis C virus · Transfusion transmission · Safe blood HCV testing

✉ Manal A.-M. Antonios
malakmanal@yahoo.com

Ahmed El-Nawawy
Dr_anawawy@yahoo.com

Shams Abdel-Fattah Arafa
shamsarafa@hotmail.com

Adham Ahmed Badeib
limaadham@yahoo.com

¹ Department of Pediatrics, Faculty of Medicine, El-Shatby Hospital, Alexandria University, Alexandria, Egypt

² Faculty of Medicine, Alexandria University, Alexandria, Egypt

Introduction

Egypt has the highest prevalence of Hepatitis C Virus (HCV) in the world, estimated nationally at 14.7% [1]. Many individuals living with HCV are unaware of their infectious status [2]. Therefore, receipt of HCV-infected blood transfusions remains an important source of infection [3]. In general, the main screening assay for detecting anti-HCV is the enzyme immunoassay (EIA). However, one of the major risk factor causing HCV-transfusion transmission is the so-called “window period” during which the antibody tests are unable to identify subjects where the virus is present in plasma in large quantities while antibodies have not yet been produced [4]. Therefore, in the acute stage, anti-HCV reactivity may remain undetectable for several months even by the most sensitive assays [5].

In Egypt, HCV screening of donor blood through national protocols mandates only HCV antibodies detection by EIA [6]. While, Alexandria University blood bank adopted double screening tests: a fully automated chemiluminescence immunoassay followed by Nucleic Acid Testing (NAT). The aim of the present study was to assess the efficiency of this dual check of HCV in preventing transfusion related infection among patients admitted to Alexandria Pediatric Intensive Care Unit (PICU).

Subjects and Methods

A prospective cohort study was designed after obtaining an informed consent from caregivers of patients admitted to PICU during 6 months period starting from first of October 2017. All admitted cases to the PICU were screened and those having past history of HCV infection or treatment or at risk of acquiring HCV from previous blood donation,

dialysis, surgery, or HCV positive mothers were excluded. The included patients were subjected to routine laboratory and clinical data collection and performed HCV RNA detection on admission by conventional reverse transcriptase polymerase chain reaction (RT-PCR) technique. Only negative cases were recruited, then the group of patients who were candidates for blood or blood products transfusion during their PICU stay were followed up after 4 weeks from discharge to repeat RT-PCR for HCV RNA detection.

Sample Size

Based on Prati review [7], a sample size of 33 patients was estimated enough required sample as statistically significant with 80% power and at a significance level of 95% (alpha error = 0.05) for a pilot study. Sample size was calculated using MedCalc Statistical Software version 14.8.1.

RT-PCR Detection Technique Steps

1. RNA extraction from serum using QIA amp viral RNA Qiagen kit according to the manufacturer instructions.
2. C DNA synthesis was generated from RNA template using ready to go RT-PCR beads (GE healthcare). Ready-to-go RT-PCR utilize Moloney Murine Leukemia Virus (M-Mul. V) reverse transcriptase and Taq DNA polymerase to generate PCR.
3. Nested primers based on highly conserved 5'-non-coding region where the sequences of the outer primers (1CH-2CH) and the inner primers (i TS-4CH).

Results

Figure 1 shows the flow-diagram summarizing the recruitment strategy of the studied population, and Table 1 shows the comparison between transfused and non-transfused patients. The data showed that patients presenting with sepsis or gastrointestinal diseases were more in need for transfusion therapy. Transfused patients had significantly more days of PICU stay and their death rate was significantly higher than non-transfused patients.

A total of 33 patients received 108 transfusions: 53 times plasma, 34 packed red blood cells, and 21 times platelets. Nine patients of them deceased during PICU stay and the remaining 24 patients were all found to be negative for RT-PCR at follow-up after 4 weeks from PICU discharge.

Fig. 1 RECORD flow-diagram of the strategy of recruitment of the studied population

Discussion

Developed countries have successfully implemented stringent donor screening, voluntary blood donation and advanced sensitivities of technologies for blood donation screening to reach acceptable levels of blood safety [8]. Blood safety presents a serious challenge in Egypt, having the highest recorded prevalence of HCV in the world [9]. The anti-HCV assays used for screening HCV infection in most Egyptian blood banks seems inadequate because most anti-HCV antibodies do not correlate well with viremia [10]. Second/third generation HCV antibody screening EIAs coupled with HCV RNA detection by NAT has resulted in marked reduction in transfusion transmission risk [8]. The Alexandria University blood bank adopted dual technique of HCV screening (PRISM, Abbott® anti-HCV immunoassay) followed by NAT (Procleix® Ultrio Elite, version: 2.4.5 NOVARTIS®) with a very high sensitivity ranging from 96 to 99.96% in literature [11, 12]. This meticulous screening has resulted in the not-astronomical results of the current study where no patients acquired HCV infection even after multi-transfusion. This is in accordance with many studies that stated that when both measures are associated, the risk of HCV infection post transfusion becomes negligible close to 0.1 per million blood supplies [8, 13, 14].

Table 1 Comparison between transfused and non-transfused patients

	Blood transfusion				Test of sig.	<i>p</i>
	Transfused (n = 33)		Non-transfused (n = 35)			
	No	%	No	%		
<hr/>						
<i>Age (months)</i>						
Min–max	5.00–96.0		1.00–168.0		Z = 1.959	0.050
Mean (SD)	10.99 (16.43)		33.17 (44.45)			
Median (IQR)	6.0 (3–13)		13.0 (4–72)			
<i>Sex</i>						
Male	19	57.6	19	54.3	$\chi^2 = 0.075$	^{FE} <i>p</i> = 0.758
Female	14	42.4	16	45.7		
<i>PIM 2 score</i>						
Min–max	4.60–97.0		3.50–99.0		Z = 0.976	0.329
Mean (SD)	54.65 (23.01)		50.66 (25.15)			
Median (IQR)	64.0 (40.2–70)		50.0 (32.3–66)			
<i>Disease category^a</i>						
GIT cases	20	60.6	11	31.4	$\chi^2 = 5.829^*$	^{FE} <i>p</i> = 0.016*
Respiratory cases	6	18.2	10	28.6	$\chi^2 = 1.019$	^{FE} <i>p</i> = 0.313
Renal cases	4	12.1	3	8.6	$\chi^2 = 0.232$	^{FE} <i>p</i> = 0.705
Cardiac cases	15	45.5	13	37.1	$\chi^2 = 0.484$	^{FE} <i>p</i> = 0.486
Sepsis cases	21	63.6	9	25.7	$\chi^2 = 9.908^*$	^{FE} <i>p</i> = 0.002*
DKA cases	0	0.0	3	8.6	$\chi^2 = 2.959$	^{FE} <i>p</i> = 0.239
Drug toxicity cases	0	0.0	2	5.7	$\chi^2 = 1.943$	^{FE} <i>p</i> = 0.493
Hematology cases	4	12.1	1	2.9	$\chi^2 = 2.140$	^{FE} <i>p</i> = 0.191
Neurology cases	13	39.4	13	37.1	$\chi^2 = 0.036$	^{FE} <i>p</i> = 0.849
<i>Length of PICU stay (days)</i>						
Min–max	1.0–28.0		1.0–20.0		Z = 3.321*	0.001*
Mean (SD)	9.21 (5.82)		5.14 (4.52)			
Median (IQR)	10.0 (4–13)		4.0 (2–6)			
<i>Fate</i>						
Deceased	9	27.27	2	5.7	$\chi^2 = 7.066^*$	^{FE} <i>p</i> = 0.008*
Discharged	24	72.73	33	94.3		

ZZ for Mann Whitney test, χ^2 Chi square test, *FE* fisher exact for Chi square test, *SD* standard deviation, *IQR* interquartile range, *PIM 2* pediatric index of mortality, *GIT* gastrointestinal tract, *DKA* diabetic ketoacidosis

*Statistically significant at *p* ≤ 0.05

^aOne patient may have more than one disease category

In 2015, Egypt launched an ambitious national HCV treatment program aiming to treat over 250,000 chronically infected individuals per year with the goal to reach a prevalence < 2% by 2025. Despite this progress, existing evidence suggests ongoing HCV transmission in Egypt, and medical care seems to be the primary source of past and present HCV transmission [15]. That is why screening of blood donations is of utmost importance especially in critically ill pediatric patients whose clinical condition is significantly worse than non-transfused patients as evidenced in Table 1 with a higher Pediatric Index of Mortality (PIM-2) score, a longer length of stay and a higher

mortality rate. These patients deserves all effort to prevent blood-borne HCV in order to avoid further complications to their originally critical situation.

Conclusion

The dual screening of HCV using serological licensed EIA and NAT should be implemented in all blood banks of Egypt together with a meticulous reporting of donors proved to be HCV positive for receiving adequate

treatment and this could be an integral part of the current Egyptian National Screening program for HCV infection.

Author contributions AEN responsible for research idea, draft revision. MAMA revision of the collected data and results, the manuscript writing. SAFA microbiological assessment. AAB collection of data.

Compliance with Ethical Standards

Conflict of interest All authors of this article declare no conflict of interest and all of them declare that they did not receive any financial support.

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