CHAPTER I

INTRODUCTION

The hepatitis C virus (HCV) was discovered in 1989 (1) and has been identified as the major etiologic agent causing most cases of posttransfusion non-A, non-B hepatitis (NANBH) worldwide (2). HCV is transmitted mainly by parenteral route via blood transfusion or sharing of contaminated needles. Exposure to NANBH/HCV is often clinically mild or subclinical during acute infection, but it has a high propensity to cause chronic hepatitis, which could progress to cirrhosis and then to liver failure (3). Furthermore, a significant association between persistant HCV infection and the development of hepatocellular carcinoma has been reported (4). Once hepatitis C infection becomes associated with serious chronic liver disease, elimination of HCV contaminated blood to prevent the risk of posttransfusion hepatitis C is thus important.

Before the availability of specific serologic assays, serum alanine amino transferase (ALT) and/or antibody to hepatitis B core antigen (anti-HBc) were used in donor screening as surrogate markers to reject donor at risk of transmitting NANBH/HCV (5,6). However, because of their nonspecificity and problems associated with donor counseling, the value of these surrogate screening has remained controversial. The specific assays for detection of antibodies to HCV-coded protein have been developed during the last few year. Detection of anti-HCV antibodies by either enzyme linked immunosorbent assay (ELISA) screening or recombinant immunoblot assay (RIBA) confirmatory tests have been widely used in routine testing of blood donations to prevent transfusion transmitted HCV infection. Although screening of blood donors with these assays has almost eleminated cases of posttransfusion hepatitis C, the detection of antibodies to HCV by ELISA and RIBA

is an indirect markers of HCV infection. They do not discriminate between on-going or resolved HCV infection. In the absence of an in vitro system to isolate the virus or a serological assay to identify HCV antigens, HCV infection can be diagnosed only by specific detection of HCV RNA using nucleic acid amplifying such as polymerase chain reaction (PCR).

In Thailand, in order to prevent posttransfusion hepatitis (PTH), the National Blood Center, Thai Red Cross Society (NBC, TRCS) has started to screen donated blood for hepatitis B virus (HBV) since 1971. Then, it became evident that NANBH/HCV posed a significant risk to recipients receiving blood transfusion. To reduce the risk of transmitting HCV, screening of blood donations for anti-HCV with a second-generation ELISA (Abbott) began in 1991. The anti-HCV positive rate among blood donors is about 1.5%. At the same time, blood chemistry tests (such as sugar, cholesterol, ALT, AST ,etc), as a complementary service, have been done for donors who requested or for those aged over 40 years. Blood units with positive anti-HCV antibodies or with ALT of higher than 100 IU/ml are excluded from transfusion. Along with such development in blood screening, cases with PTH are rarely reported. However, the specificity of anti-HCV screening in volunteer blood donors has been questioned. Moreover, recent study of HCV RNA by PCR revealed seronegative donors who donated blood during acute infection and were able to transmit HCV to the recipients (7,8,9). Several were also noted an association between the detection of HCV RNA and abnormal ALT level (10,11).

Therefore, the purpose of this study is to develop Nested RT-PCR for the detection of the presence of HCV RNA in blood donors. The results will be used to evaluate the efficiency of the screening policy and to assess the residual value of ALT testing as a complement to anti-HCV screening in preventing transmission of hepatitis C virus through blood transfusion.