CHAPTER V
DISCUSSION AND CONCLUSION

The rate of HCMV infection varies according to populations and age groups [32]. The prevalence of HCMV infection in Southeast Asian population is higher than in western countries [94]. In this study, it was decided not to test HCMV serology in mothers as previous reports described that almost 100% of Thai pregnant women have IgG antibodies against HCMV [32-35, 95]. Furthermore, most of women in this study have a low socioeconomic status, factor known to be associated with high rate of HCMV infection.

In Thailand, two studies conducted in non HIV infected pregnant women reported a rate of congenital HCMV infection of 12 and 33%; definition of congenital infection being based on detection of IgM within 3 weeks or 5 months, respectively. No report on rate of congenital HCMV infection has been reported in HIV-1 infected mothers. This report shows that within 2 weeks of life, the rate of congenital HCMV infection in HIV-1 infected infants is higher than in HIV-1 uninfected infants (17% vs. 5%, $p = 0.012$). These results are similar to those described by Chandwani et al. with congenital HCMV infection occurring in 1 of 5 HIV infected children (20%) and 0 of 19 HIV uninfected children (0%) born to HIV infected mothers in USA. However, in another study also conducted in USA, the rate of congenital HCMV infection was similar in HIV-1 infected (4.3%) and HIV-1 uninfected infants (4.5%).

The higher rate of congenital transmission in the group of HIV-1 infected infants might be due to a higher level of HCMV shedding in HIV-1 transmitted women or an impaired immuno-surveillance in HIV-1 infected infants.

In this study, 85% of HIV-1 infected infants were co-infected with HCMV within 18 months of age. This prevalence is close to those reported in children aged from 3-112 months by Temchareon et al [65] and in children aged between 13-36 months by Likitnukul et al [29], 77% and 89%, respectively. These prevalences are much higher than those reported in HIV infected children in USA by Chandwani et al

[62] and by Kovacs [13], 31% and 40%, respectively. The higher rate of HCMV infection in Thai infants may result from a higher prevalence in adult population and lower socio-economic status in Thailand than in USA.

This study has allowed to identify two risk factors for HCMV transmission to both HIV infected infants and HIV uninfected infants born to HIV-1 infected mothers, vaginal delivery and low birth weight. The transmission may occur more easily during vaginal delivery as the result of mixing of maternal and fetal blood during contractions, or contamination through mucous membrane, or via ingestion of infected maternal blood or cervico-vaginal secretions when the fetus passes through the birth canal.

This study shows for the first time that a low birth weight is a risk factor for HCMV transmission in HIV-1 infected infants. Infants with low birth weight (<2,910 g) are at higher risk of being infected by HCMV may be because of impaired health or prematurity. Furthermore, the results show that the rate of HCMV infection in infants born to mother with less than 39 weeks of gestational age at delivery tend to be higher than in those born to mothers with mature pregnancy .

These two risk factors were not studied by Fowler and Pass who reported other risk factors such as the occurrence of any STDs during pregnancy, and maternal age <25 years [96]. These two factors were analysed in the present study but were not found associated with HCMV transmission. The difference observed in the two studies may be due to the populations studied, normal pregnant women in Fowler's study and HIV infected pregnant women in this study. Also, women participating in Fowler's study were American who may acquire primary HCMV infection during early adulthood. Thus, younger women would be more at risk to transmit infection during that period. In Thailand, it is likely that the effect of young age during pregnancy cannot be demonstrated as most pregnant women are already infected by HCMV during early childhood.

HIV-1 infected infants with CD4+ T cell count below 340 cells/μL before initiation of antiretroviral treatment tend to have a higher rate of HCMV infection than infants with high CD4+ T cell count. This result is concordant to Kovacs et al.'s study which showed that the mean of CD4+ T cell counts at 15 months of age was lower in HCMV/HIV-1 co-infected infants than in infants with HIV-1 infection only.

Association between HCMV infection and disease progression in HIV infected infants is still unclear. Indeed, some studies described an association between HCMV infection and a more rapid progression to HIV disease in both children [13] and adults [11, 12, 14, 45] while other studies did not confirm this association [43, 49-51, 59]. The present study did not find any significant association between HCMV/HIV co-infection and disease progression in HIV infected children. This finding is similar to the report from Kitchen et al [59] who described in a cohort study of 273 HIV infected children, a similar survival rate in HCMV/HIV co-infected children and HIV infected only but children had a median age of 9 years (range, 0.6 to 21 years). However, a difference in the rate of disease progression was reported by Kovacs et al. One hypothesis to explain the difference with the report from Kovacs et al [13] could be the number of HIV infected infants followed. Indeed, in Kovacs study [13], the ratio of HCMV/HIV co-infected infants to HIV infected only was 40/23 while in this study it was 72/13. The low number of HIV infected infants in this study may thus affect the result of analysis. In addition, the number of infants who progressed to disease was much higher in this study than in Kovacs study, 44 of 72 co-infected infants and 6 of 13 HIV infected only versus 28 of 40 and 7 of 23, respectively. In Kovacs study [13], no information about maternal CD4+ T cells was provided which does not allow the comparison of maternal immune status between the 2 studies.

Other factors such as host genetic susceptibility [97] (e.g. CCR5, CCR2, SDF-1) and other viral co-infections [98] (e.g. HBV, HCV, HHV-8) have been associated with HIV disease progression in HIV-1 infected individuals and are currently under investigation.

In conclusion, this study shows that HIV infected infants are more at risk of being infected by HCMV than HIV uninfected infants whatever their age. HCMV infection occurs earlier in HIV infected infants. This study has identified 2 risk factors for HCMV mother-to child transmission which are a vaginal delivery and a low birth weight. Furthermore, being HCMV co-infected does not seem to represent a risk factor for a more rapid disease progression in HIV infected infants. This result should be taken with caution as the number of infants infected with HIV-1 only was low compared to the number of HIV-1/HCMV co-infected infants. Additional studies are needed to confirm this result.