RESULTS

Over a period of 4.5 months, twenty-six male and twenty-five female neonates admitted to the Neonatal Intensive Care Unit (NICU), Newborn 3 and Newborn 4 ward of the Department of Pediatric were prescribed gentamicin for suspected of bacterial infections. One female patient with polycystic kidney disease was excluded, thus, the number of neonates enrolled in this study were fifty. The demographic characteristics and the diagnosis of the neonatal patients are shown in Tables 9 and 10, respectively. The numbers of neonates in each group were 10, 10, 14 and 16, respectively. Their average gestational ages and their average weights were 27.0 $\pm$ 2.1, 31.1 $\pm$ 1.2, 35.6 $\pm$ 1.3, 39.6 $\pm$ 1.3 weeks and 0.77 $\pm$ 0.29, 1.35 $\pm$ 0.26, 2.39 $\pm$ 0.37, 3.10 $\pm$ 0.48 kg for neonates in groups I, II, III, and IV, respectively. We enrolled both the preterm and term neonates with the youngest and the oldest gestational age of 24 weeks and 41 weeks, respectively. The lowest birth weight was 0.41 kg while the highest value was 3.97 kg. Their postnatal ages were 1 day for neonates in group I-III and ranged from 1-8 days for neonates in group IV. The most common indication of gentamicin was respiratory distress syndrome (RDS), while, the second and the third common diagnoses were premature rupture of the membranes (PROM) and suspected pneumonia, respectively. RDS had been diagnosed in 17/20 in neonates with GA $\leq$ 29 - 33 weeks while this disease was decrease to 8/30 for older neonates with GA 34 – $\geq$ 38 weeks. The mean hemoglobin and hematocrit levels of the neonates were within the normal range, but the mean white blood cell count in neonates with GA of 34-37 weeks and $\geq$ 38 weeks were higher than normal range. This finding suggested the possibility of bacterial infection. The Apgar score at 5 minutes were within normal value (range from 6-10). The result of all blood cultures obtained from our neonatal patients showed no growth of organism after 1 week. Table 11 shows the dose and duration of gentamicin administration, while Table 12 shows lists of concurrent medication. The average doses of gentamicin were 3.70 $\pm$ 1.09, 6.08 $\pm$ 1.12, 9.40 $\pm$ 1.38 mg and 12.10 $\pm$ 1.81, whereas the duration of gentamicin administrations were 5.1 $\pm$ 2.3, 5.4 $\pm$ 2.6, 7.1 $\pm$ 2.7 and 6.0 $\pm$ 1.7 days, for neonates in groups I, II, III and IV, respectively. The synergistic

antibiotic ampicillin was given to all cases. Eight cases received concurrent indomethacin and one case received ibuprofen for closure of hemodynamically significant PDA. A small number of patients (11cases) received concurrent potential nephrotoxic medication (furosemide, indomethacin) and one case required dopamine infusion to maintain stable cardiovascular status. The list of concurrent medications given to patients with gestational age $\leq$ 29 weeks admitted to the NICU was more than the other groups.

Table 9. Demographic data of neonatal patients.

Characteristic	Gestational age (weeks)			
	≤29	30-33	34-37	≥38
N	10	10	14	16
Sex (male/female)	3/7	6/4	8/6	9/7
Gestational age (weeks)	27.00 ± 2.06[a] (24-29)[b]	31.30 ± 1.16 (30-33)	35.57 ± 1.28 (34-37)	39.56 ± 1.31 (38-41)
Postnatal age (days)	1	1	1	1.6 ± 1.8 (1-8)
Weight (kg)	0.77 ± 0.29 (0.41-1.19)	1.35 ± 0.26 (1.00-1.79)	2.39 ± 0.37 (1.50-2.87)	3.10 ± 0.48 (2.30-3.97)
Height (cm)	32.70 ± 4.40 (29-38)	39.22 ± 1.99 (37-42)	45.46 ± 2.52 (40-50)	49.34 ± 2.80 (44-56)
BSA (m^2)	0.08 ± 0.02 (0.06-0.11)	0.11 ± 0.02 (0.07-0.14)	0.17 ± 0.02 (0.12-0.19)	0.20 ± 0.02 (0.16-0.23)
Apgar score at 5 minutes	8[c] (7-10)	10[c] (6-10)	10[c] (8-10)	10[c] (7-10)
Hemoglobin (g/dl) (normal 10-15)	14.60 ± 2.24 (12.1-18.6)	16.48 ± 3.41 (11.5-22.5)	17.75 ± 2.97 (12.8-23)	15.88 ± 2.57 (10.6-19.3)
Hematocrit (%) (normal 40-50)	46.81 ± 7.06 (39.5-59.9)	50.55 ± 9.97 (36.3-69.2)	54.21 ± 9.20 (39.4-70)	49.38 ± 8.74 (31.9-58.2)
WBC (/ul) (normal 5-10x10^3)	11.03x10^3 ± 2.9x10^3 (7,600-15,800)	10.64x10^3 ± 4.3x10^3 (5,200-17,800)	20.38x10^3 ± 7.1x10^3 (8,700-30,900)	20.99x10^3 ± 9.1x10^3 (7,500-38,800)

[a] Present as mean ± SD

[b] Present as range

[c] Present as mode

Table 10. Indication of gentamicin in neonatal patients at stdy entry.

Diagnosis	Frequency of cases according to gestational age			
	≤ 29 weeks	30-33 weeks	34-37 weeks	≥ 38 weeks
RDS[a]	9	8	3	5
PROM[b]	0	3	8	3
Suspected pneumonia	1	1	7	3
Suspected MAS[c]	4	0	1	6
TTNB[d]	0	2	1	0
Suspected sepsis	0	0	3	0
Pneumothorax	0	0	0	2

[a] Respiratory distress syndrome

[b] Premature rupture of the membrane

[c] Meconium aspiration syndrome

[d] Transient tachypnea of the newborm

Table 11. Dose and duration of gentamicin administration in each group of neonatal patients.

Gestational age (weeks)	Gentamicin	
	Dose (mg)	Duration (days)
≤29	3.70 ± 1.09 (2.2-5.0)	5.1 ± 2.3 (1-7)
30-33	6.08 ± 1.12 (4.5-8.0)	5.4 ± 2.6 (1-7)
34-37	9.40 ± 1.38 (7.5-11.0)	7.1 ± 2.7 (3-11)
≥38	12.10 ± 1.81 (9.0-15.0)	6.0 ± 1.7 (3-7)

Present as mean ± SD and range

Table 12. Concurrent drug administrations with gentamicin in each group of neonatal patients.

Drug	Frequency of case according to gestational age			
	≤ 29 weeks	30-33 weeks	34-37 weeks	≥ 38 weeks
Ampicillin	10	10	14	16
Indomethacin	4	4	0	0
10% calcium gluconate	4	3	0	0
Survanta™	5	0	0	0
Ranitidine	3	1	0	0
Furosemide	1	1	0	1
Zidovudine	0	0	1	2
Dopamine	1	0	0	0
Metronidazole	1	0	0	0
Aminophylline	1	0	0	0
Ibuprofen	0	1	0	0
Nevirapine	0	0	0	1

Gentamicin was given as a slow intravenous infusion over a period of 31.26 ± 3.33 minutes (mean ± SD) via an infusion pump. The sampling times of the peak and the trough concentrations are shown in Table 13. The average sampling times for the peak concentrations were 34.8, 31.1 and 32.4 minutes for the 1st, the 3rd and the 6th doses, respectively. Average sampling times for the trough concentrations were 32.2 and 36.0 minutes before the 3rd and the 6th doses, respectively. The initial peak concentration of Patient no. 7 (GA 34-37 weeks) was missing and Patient no. 12 (GA ≥ 38 weeks) received incorrect dose of gentamicin, therefore, their initial peak concentrations were excluded. The peak and trough concentrations of the third dose of Patient no.5 (GA 34-37 weeks) were also excluded because of wrong sampling times. The peak and trough concentrations of the sixth dose of patient no. 15 (GA ≥ 38 weeks) were excluded because of wrong dose. Two neonates in group II (GA 30-33 weeks) received gentamicin and the medication was stop and switched to cefotaxime after drawing of the initial peak concentration.

Table 13. Time to sampling in all patients.

Peak concentration	**Sampling time (minutes)**
First dose	34.76 ± 11.50
Third dose	31.05 ± 6.55
Sixth dose	32.38 ± 8.76
Trough concentration	**Sampling time (minutes)**
Before third dose	32.19 ± 8.41
Before sixth dose	36.00 ± 7.97

Present as mean ± SD and range

Table 14. The number of neonates receiving the 1st, the 3rd and the 6th doses of gentamicin in each group of neonatal patients.

Dose	**Gestational age (weeks)**			
	≤ 29	**30-33**	**34-37**	**≥38**
First dose	Day 1 (n =10)	Day 1 (n =10)	Day 1 (n =14)	Day 1 (n =16)
Third dose	Day 5 (n = 6)	Day 5 (n = 7)	Day 4 (n =12)	Day 3 (n =16)
Sixth dose	Day 11 (n = 0)	Day 11 (n = 0)	Day 8 (n = 5)	Day 6 (n =11)

The number of neonates receiving the 1st, the 3rd and the 6th doses in each group is shown in Table 14. The 3rd dose of gentamicin was indicated only in 13 out of 20 neonates with GA < 33 weeks, while this dose was continued in 28 out of 30 neonates with GA 34 - ≥38 weeks. The 6th dose of gentamicin was given only to 16 out of 30 neonates with GA 34 - ≥38 weeks.

Figure 5, 6 and 7 depicts the initial peak concentrations, the peak concentrations after the 3rd dose and the 6th doses, respectively. Figures 8 and 9 depicts the trough concentrations before the 3rd dose and the 6th doses, respectively.

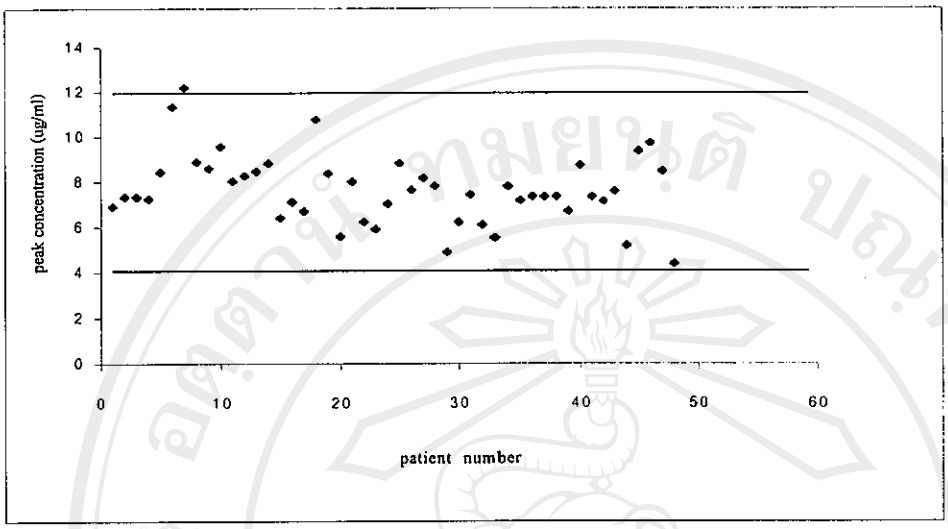

Figure 5. The plot of individual initial peak concentrations of gentamicin (n=48). The horizontal lines represent the desired therapeutic range.

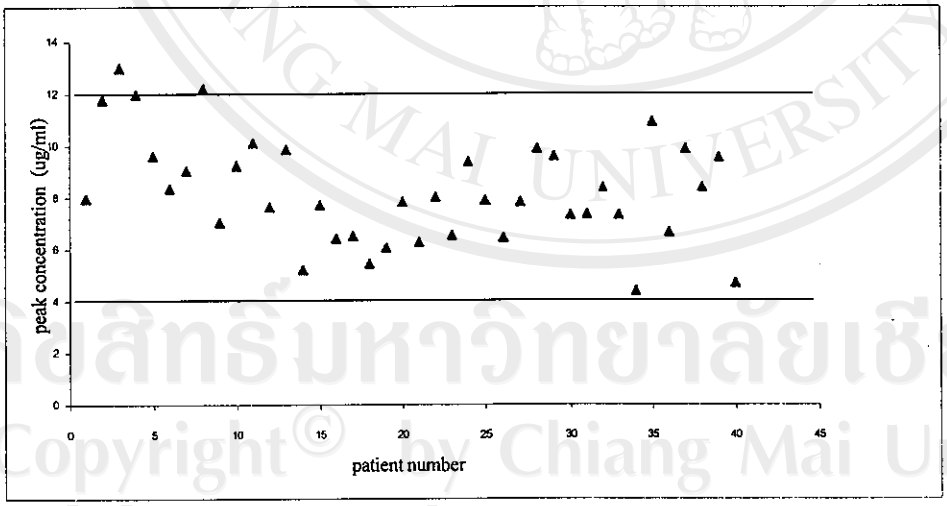

Figure 6. The plot of individual peak gentamicin concentrations after the 3rd dose (n=40). The horizontal lines represent the desired therapeutic range.

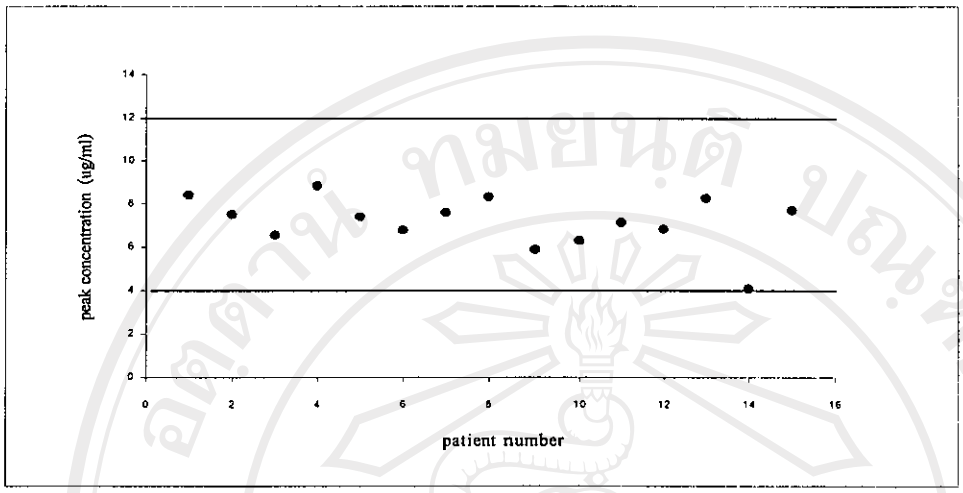

Figure 7. The plot of individual peak gentamicin concentrations after the 6th dose (n=15). The horizontal lines represent the desired therapeutic range.

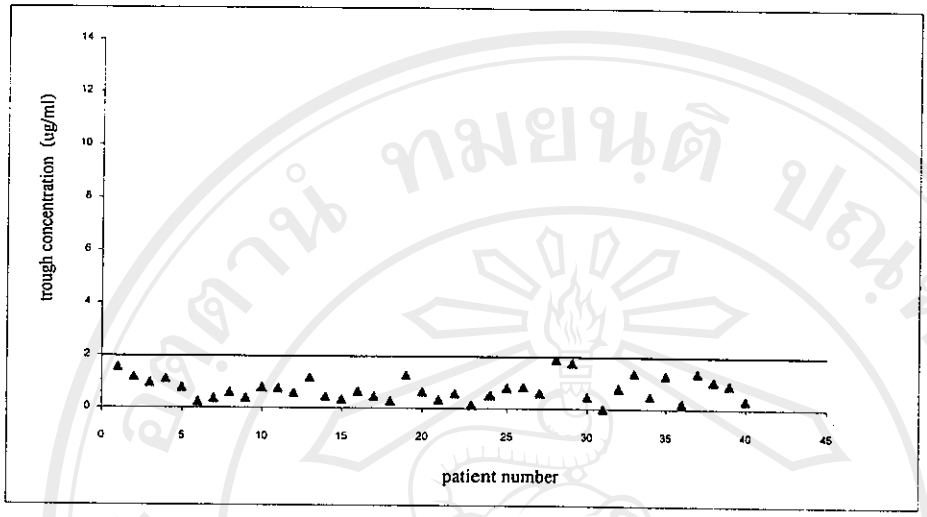

Figure 8. The plot of individual trough gentamicin concentrations before the 3rd dose (n=40). The horizontal lines represent the concentration to be avoided.

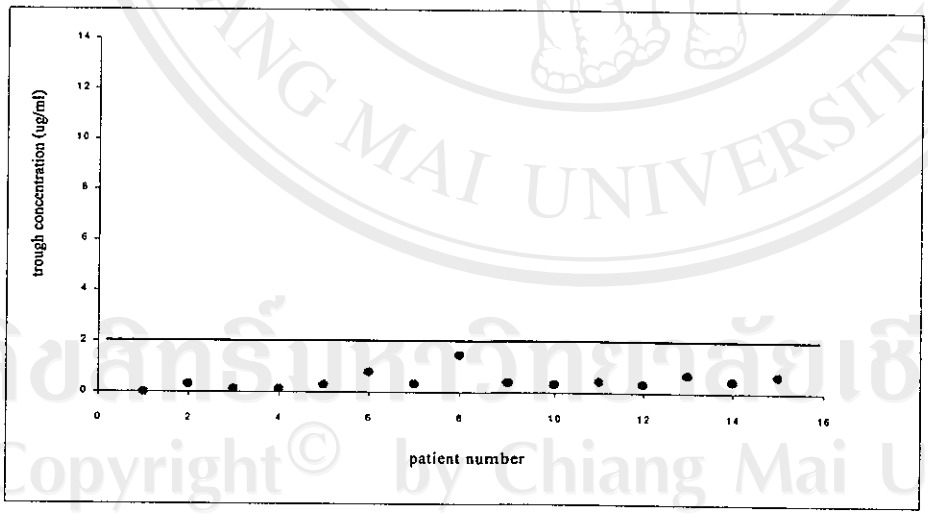

Figure 9. The plot of individual trough gentamicin concentrations before the 6th dose (n=15). The horizontal lines represent the concentration to be avoided.

Table 15 illustrates the mean peak concentrations after the 1st, the 3rd and the 6th doses of neonates in each group. Tables 16-18 illustrate the number of neonates whose gentamicin concentrations were within the therapeutic range, less than or higher than the therapeutic range after the 1st, the 3rd and the 6th doses, respectively.

Table 15. Average gentamicin peak concentrations after the 1st, the 3rd and the 6th doses of gentamicin in each group of neonatal patients.

Gestational age	**Peak concentration (ug/ml)**		
(weeks)	**At 1st dose**	**At 3rd dose**	**At 6th dose**
≤29	8.80 ± 1.80 (6.92-12.21)	10.45 ± 2.08 (7.97-13.00)	NA
30-33	7.86 ± 1.47 (5.59-10.78)	9.32 ± 1.69 (7.06-12.20)	NA
34-37	6.92 ± 1.18 (4.91-8.84)	6.86 ± 1.24 (5.22-9.39)	7.74 ± 0.90 (6.55-8.83)
≥38	7.45 ± 1.39 (4.40-9.74)	7.92 ± 0.90 (4.40-10.92)	6.89 ± 1.26 (4.09-8.31)

Present as mean ± SD and range

NA = not applicable

Table 16. The number of neonatal patients whose gentamicin concentrations were less than, within or higher than the therapeutic range of 4-12 ug/ml after the 1st dose.

Gestational age (weeks)	Numbers of neonates with specified gentamicin concentration		
	< 4 ug/ml	4-12 ug/ml	> 12 ug/ml
≤29	0	9/10	1[a]/10
30-33	0	10/10	0
34-37	0	13/13	0
≥38	0	15/15	0

[a] gentamicin concentration = 12.21 ug/ml

Table 17. The numbers of neonatal patients whose gentamicin concentrations were less than, within or higher than the therapeutic range of 4-12 ug/ml after the 3rd dose.

Gestational age (weeks)	Numbers of neonates with specified gentamicin concentration		
	< 4 ug/ml	4-12 ug/ml	> 12 ug/ml
≤29	0	5/6	1[a]/6
30-33	0	6/7	1[b]/7
34-37	0	11/11	0
≥38	0	16/16	0

[a] gentamicin concentration = 13.00 ug/ml, [b] gentamicin concentration = 12.20 ug/ml

Table 18. The numbers of neonatal patients whose gentamicin concentrations were less than, within or higher than the therapeutic range of 4-12 ug/ml after the 6th dose.

Gestational age	Numbers of neonates with specified gentamicin concentration		
	< 4 ug/ml	4-12 ug/ml	> 12 ug/ml
≤29 weeks	NA	NA	NA
30-33 weeks	NA	NA	NA
34-37 weeks	0	5/5	0
≥38 weeks	0	10/10	0

NA = not applicable

The mean initial peak concentrations were 8.80 ± 1.80, 7.86 ± 1.47, 6.92 ± 1.18 and 7.45 ± 1.39 ug/ml for neonates in group I, II, III and IV, respectively. Their initial peak concentrations were within the therapeutic range of 4-12 ug/ml, except one neonate in group I whose concentration was higher than the therapeutic range (12.21 ug/ml) (Table 16). The mean peak concentrations after the 3rd dose were 10.45 ± 2.08, 9.32 ± 1.69, 6.86 ± 1.24 and 7.92 ± 1.83 ug/ml for neonates in group I, II, III and IV, respectively. Similar to the initial peak concentration, most of the maintenance peak concentrations after the 3rd dose were within the therapeutic range, except 2 neonates (13.0 and 12.2 in neonates with GA ≤ 29 and 30-33 weeks), respectively whose peak gentamicin concentrations were higher than the therapeutic level. The mean peak concentrations after the 6th dose were 7.74 ± 0.90 and 6.89 ± 1.26 ug/ml for neonates in group III and IV, respectively. All patients had peak concentrations after the 6th dose within the therapeutic range. Since gentamicin was discontinued in four neonates whose gentamicin concentrations were out of the therapeutic range, no dosage adjustment was required for the rest of the neonatal patients in this study.

Table 19 illustrates the mean gentamicin trough concentrations before the 3rd and the 6th doses of gentamicin in each group of neonatal patients. Tables 20 and 21 illustrate the number of neonates whose gentamicin concentrations were less than or higher than the safety concentration of < 2 ug/ml before the 3rd and the 6th doses, respectively.

Table 19. Average gentamicin trough concentrations before the 3rd and the 6th doses of gentamicin in each group of neonatal patients.

Gestational age (weeks)	Trough concentration (ug/ml)	
	Before 3rd dose	Before 6th dose
≤29	0.99 ± 0.41 (0.24-1.55)	NA
30-33	0.66 ± 0.27 (0.36-1.16)	NA
34-37	0.51 ± 0.29 (0.14-1.26)	0.18 ± 0.13 (0-0.33)
≥38	0.88 ± 0.54 (0-1.86)	0.61 ± 0.35 (0.34-1.49)

Present as mean ± SD and range

NA = not applicable

Table 20. The number of neonatal patients whose gentamicin concentrations were less than and higher than the safety concentration of < 2 ug/ml before the 3rd dose.

Gestational age (weeks)	Numbers of neonates with specified gentamicin concentration	
	< 2 ug/ml	> 2 ug/ml
≤29	6/6	0
30-33	7/7	0
34-37	11/11	0
≥38	15/15	0

Table 21. The number of neonatal patients whose gentamicin concentrations were less than and higher than the safety concentration of < 2 ug/ml before the 6th dose.

Gestational age (weeks)	Numbers of neonates with specified gentamicin concentration	
	< 2 ug/ml	> 2 ug/ml
≤ 29	NA	NA
30-33	NA	NA
34-37	5/5	0
≥ 38	10/10	0

NA = not applicable

The mean trough concentrations before the 3rd dose were 0.99 ± 0.41, 0.66 ± 0.27, 0.51 ± 0.29 and 0.88 ± 0.54 ug/ml for neonates in group I, II, III and IV, respectively. Only 16 neonates in group III and IV received the 6th dose and the trough concentration (ug/ml) before this dose were 0.18 ± 0.13 and 0.61 ± 0.35 ug/ml, respectively.

The measurement of gentamicin pharmacokinetic parameters such as K_e, CL, V_d and $t_{1/2}$ are summarized in Table 22 and depicte in Figures 10, 11, 12 and 13, respectively. The K_e of gentamicin were 0.069 ± 0.034, 0.068 ± 0.019, 0.109 ± 0.053 and 0.116 ± 0.054 hr^{-1} for neonates in group I, II, III and IV, respectively. Similarly, the corresponding CL of gentamicin were 0.035 ± 0.017, 0.036 ± 0.009, 0.064 ± 0.024 and 0.073 ± 0.041 L/kg/hr, respectively. V_d were 0.513 ± 0.087, 0.543 ± 0.058, 0.609 ± 0.106 and 0.621 ± 0.138 L/kg, while, the $t_{1/2}$ were 11.97 ± 4.67, 10.82 ± 2.58, 7.62 ± 2.76 and 6.70 ± 1.40 hr for neonates in group I, II, III and IV, respectively. Statistical analysis showed that the K_e, CL and $t_{1/2}$ of gentamicin for neonates in group I were not significantly different from neonates in group II, and similarly these parameters for neonates in group III were not significantly different from neonate in group IV. However, significant differences of these parameters were demonstrated when compared between neonates with GA ≤ 29 - 33 weeks to neonates with GA 34 - ≥ 38 weeks (Table 22). The result showed that the K_e and CL of neonates with GA ≤ 29-33 weeks were less than those values obtained from neonates with GA 34 - ≥ 38 weeks with *P* values of 0.013 and 0.002, respectively. As a result of a slower K_e and CL, the $t_{1/2}$ of gentamicin for neonates with GA ≤ 29-33 weeks (mean 11.4, range 4.7-19.7 hr) was longer than neonates with GA 34 - ≥ 38 weeks (7.16, 2.8-13.1 hr) with a *P* value <0.001.

Similar to other pharmacokinetic parameters, the V_d of gentamicin for neonates in group I and II were not significantly different, however, their V_d (GA $\leq$ 29-33 weeks) were significantly less than neonates in group IV (GA $\geq$ 38 weeks) with *P* value of 0.050. The V_d of neonates in group III (GA 34-37 weeks) were not significant different from those values in the other groups.

The correlation between demographic data of neonates such as GA, BW, BSA and the pharmacokinetic parameters of gentamicin; K_e, CL, V_d and $t_{1/2}$ were determined by linear regression analysis. Scatterplots and correlation analysis between GA, BW, BSA and gentamicin pharmacokinetic parameters are depicted in Figures 14 – 17, 18-21 and 22-25, respectively. The association was measured by a correlation coefficient (R^2) and a t test was used to test whether R^2 was significantly different from zero. A significant level was set at 5%. Regression analysis showed positive correlation between GA, BW and BSA with gentamicin pharmacokinetic parameters. The R^2 and *P* values between GA, BW and BSA for the K_e were R^2= 0.15, *P*= 0.005, R^2= 0.26, *P*<0.001 and R^2= 0.17, *P*=0.004, respectively. Likewise the relationship between GA, BW and BSA with CL and V_d were R^2= 0.24, *P*<0.001, R^2= 0.29, *P*<0.001, R^2= 0.26, *P*<0.001 and R^2= 0.14, *P*= 0.008, R^2= 0.15, *P*=0.005, R^2= 0.16, *P*=0.006, respectively. BW correlated best to gentamicin pharmacokinetic parameters, while GA and BSA coreelated fairly.

The serum concentrations of creatinine and BUN for neonatal patients in each group after administration of the 1st, the 3rd and the 6th doses of gentamicin were shown in Table 23 and Figures 26-27, respectively. The initial concentrations of creatinine were 1.02 $\pm$ 0.18, 0.98 $\pm$ 0.29, 0.87 $\pm$ 0.13 and 0.92 $\pm$ 0.36 mg/dl for neonates in group I, II, III and IV, respectively. The corresponding values of creatinine concentrations for neonates in each group were 1.00 $\pm$ 0.17, 0.76 $\pm$ 0.18, 0.47 $\pm$ 0.20 and 0.52 $\pm$ 0.20 mg/dl after the 3rd dose, and the creatinine values after the 6th dose were 0.48 $\pm$ 0.18 and 0.47 $\pm$ 0.11 mg/dl for neonates in group II and IV, respectively. The result showed that the initial creatinine concentrations in all groups were higher than normal values. Thereafter, the creatinine concentrations declined except for neonates in group I whose creatinine concentrations were persistently higher than upper normal value of 0.6 mg/dl. The creatinine concentrations for neonates in group III and IV (GA 34 - $\geq$ 38 weeks) declined to normal range within 3-4 days. The creatinine concentrations after the 3rd dose (Day 4 and 3) and the 6th dose (Day 8 and 6) were significantly lower than the initial concentrations for neonates in group III and IV with the *P* values of <0.001, 0.038 and <0.001, 0.008, respectively. The BUN

concentrations of the neonates in this study were within the normal range (lower than the upper normal level of 25.8 mg/dl). These values were not significantly different between the doses except in group (GA ≥ 38 weeks) whose BUN concentrations were significantly decline after the 3rd and 6th doses (P = 0.013 and 0.04, respectively). There were no complications or adverse drug reactions that were recognized in all neonatal patients in this study.

Table 22. Gentamicin pharmacokinetic parameters of neonates in each gestational age group.

Parameter	Gestational age				*P* value
	≤ 29 weeks	30-33 weeks	34-37 weeks	≥ 38 weeks	
K_e (hr^{-1})	0.069 ± 0.034*,t (0.035-0.148)	0.068 ± 0.019*,t (0.046-0.102)	0.109 ± 0.053 (0.053-0.175)	0.116 ± 0.054 (0.075-0.311)	0.013
CL (L/kg/hr)	0.035 ± 0.017*,t (0.020-0.069)	0.036 ± 0.009*,t (0.024-0.051)	0.064 ± 0.024 (0.032-0.125)	0.073 ± 0.041 (0.040-0.210)	0.002
V_d (L/kg)	0.513 ± 0.087t (0.388-0.652)	0.543 ± 0.058t (0.499-0.662)	0.609 ± 0.106 (0.499-0.840)	0.621 ± 0.138 (0.458-1.09)	0.050
$t_{1/2}$ (hr)	11.97 ± 4.67*,t (4.69-19.68)	10.82 ± 2.58*,t (6.77-15.05)	7.62 ± 2.76 (2.77-13.08)	6.70 ± 1.40 (3.52-9.24)	<0.001

Present as mean ± SD and range

ANOVA between group; the mean difference is significant at $P < 0.05$

* Significant difference from gestational age 34-37 weeks,

t Significant difference from gestational age ≥ 38 weeks

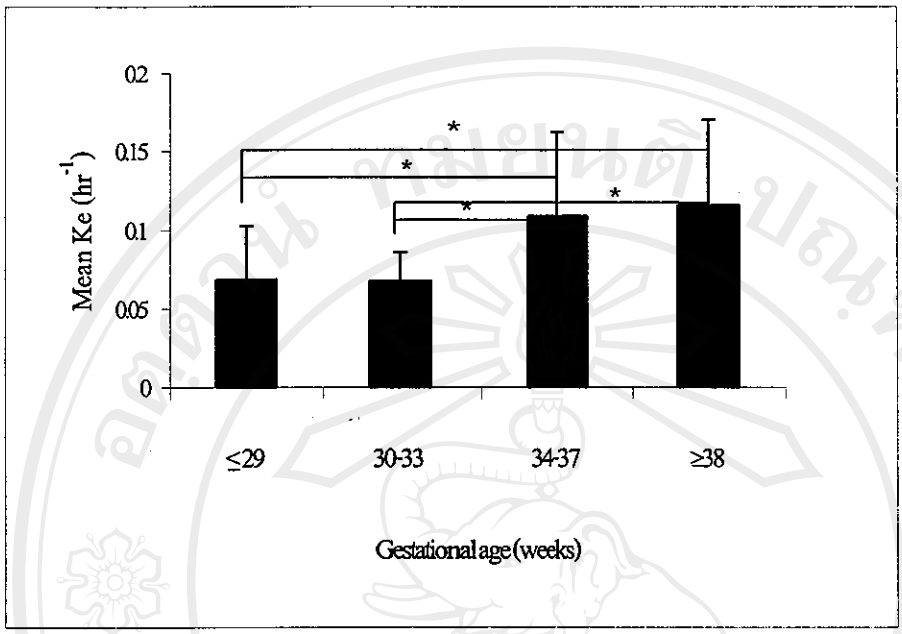

Figure 10. Mean K_e in each gestational age group. * Present significant difference at $P<0.05$

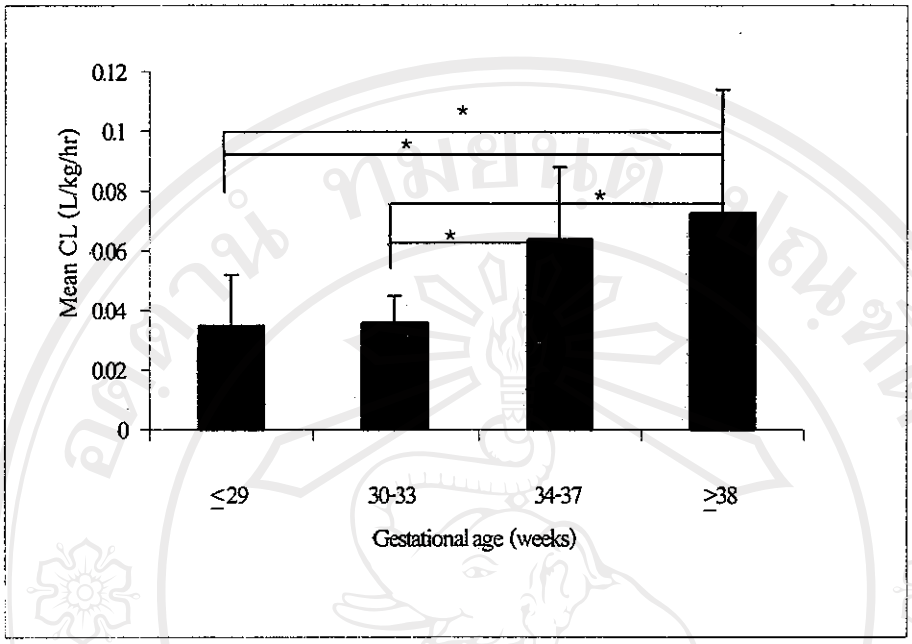

Figure 11. Mean CL in each gestational age group. * Present significant difference at $P<0.05$

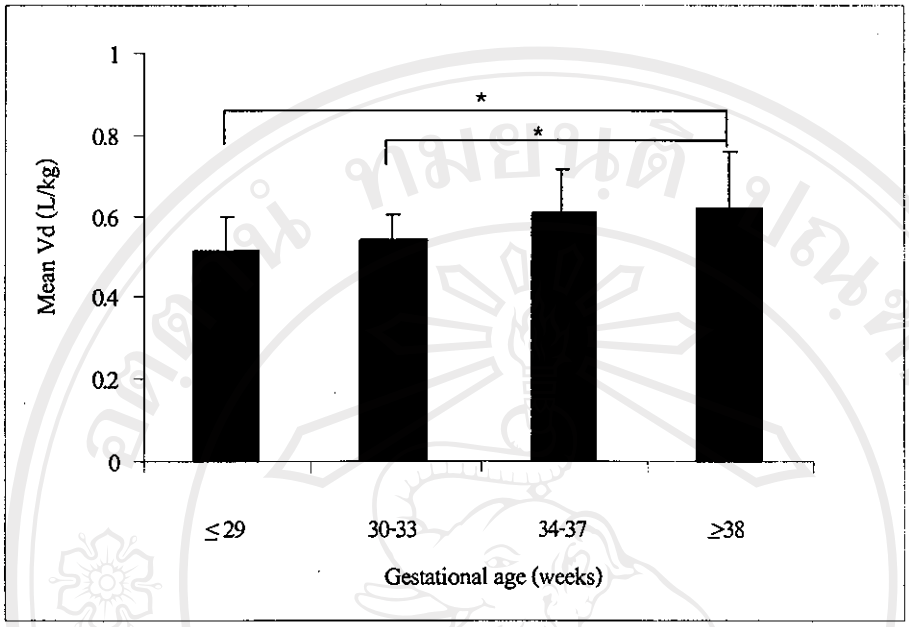

Figure 12. Mean V_d in each gestational age group. * Present significant difference at $P<0.05$

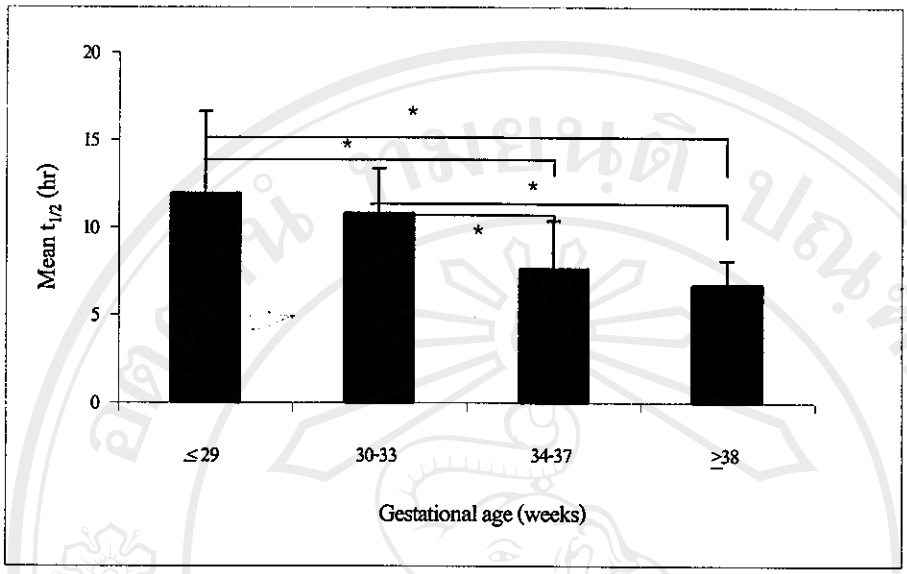

Figure 13. Mean $t_{1/2}$ in each gestational age group. * Present significant difference at $P<0.05$

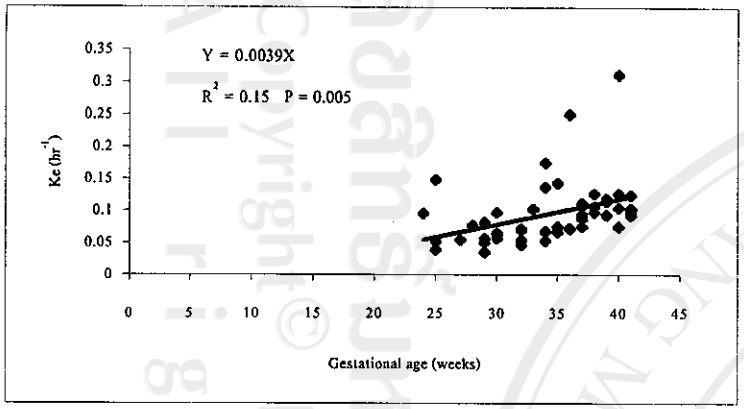

Figure 14. Correlation between GA and K_e.

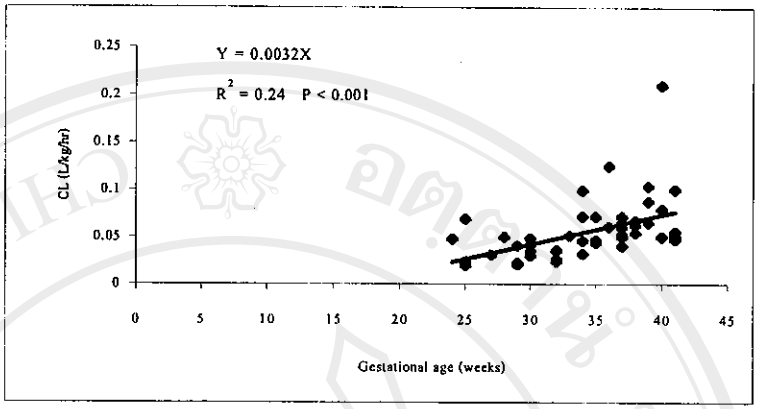

Figure 15. Correlation between GA and CL.

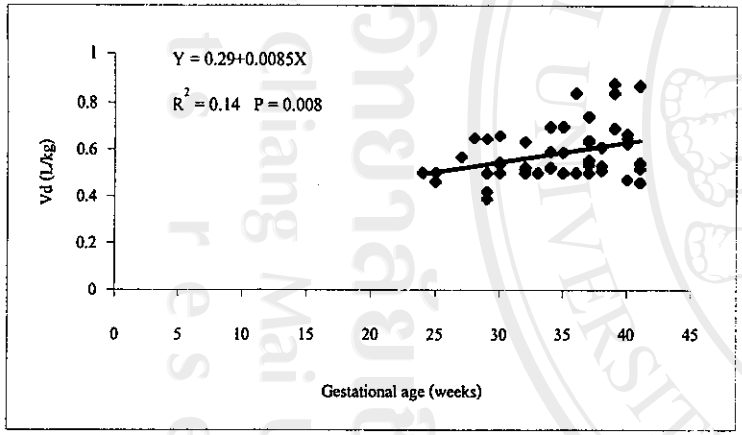

Figure 16. Correlation between GA and V_d.

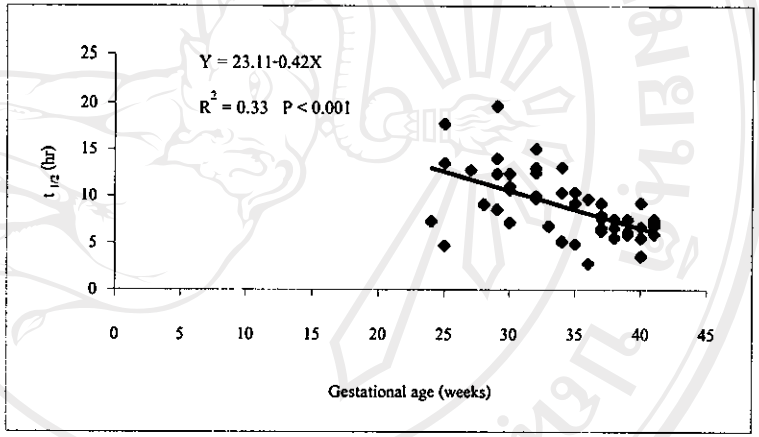

Figure 17. Correlation between GA and $t_{1/2}$.

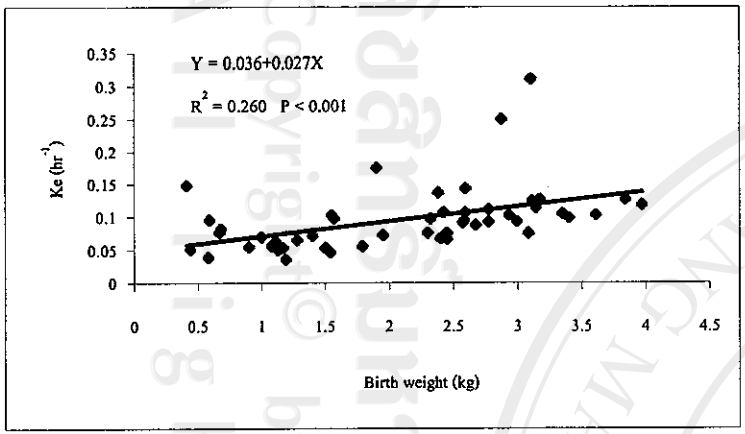

Figure 18. Correlation between Birth weight and K_e.

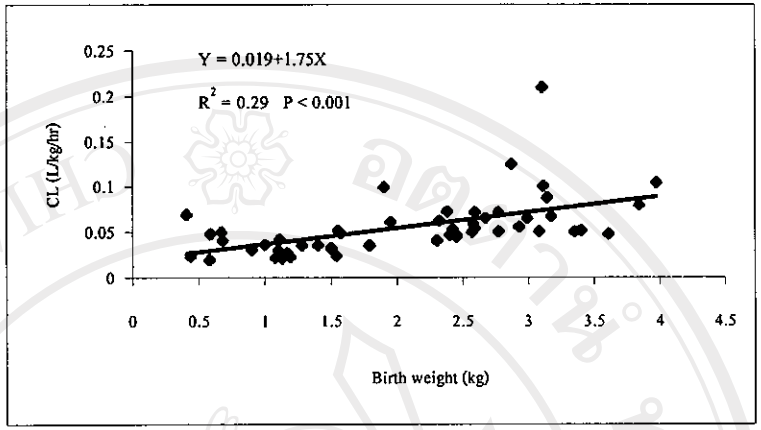

Figure 19. Correlation between Birth weight and CL.

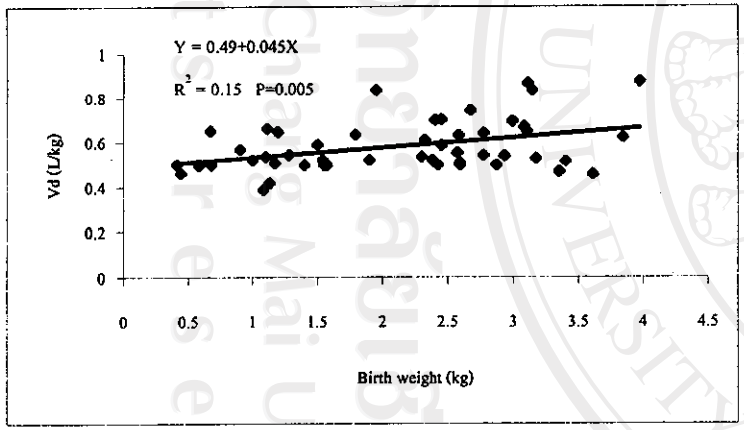

Figure 20. Correlation between Birth weight and V_d.

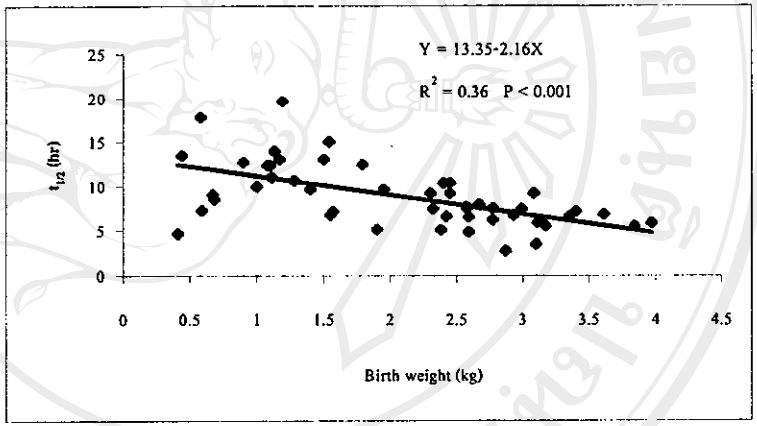

Figure 21. Correlation between Birth weight and $t_{1/2}$.

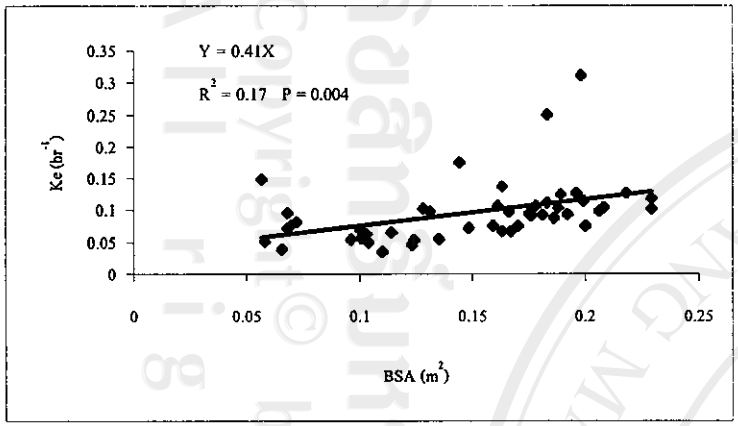

Figure 22. Correlation between BSA and K_e.

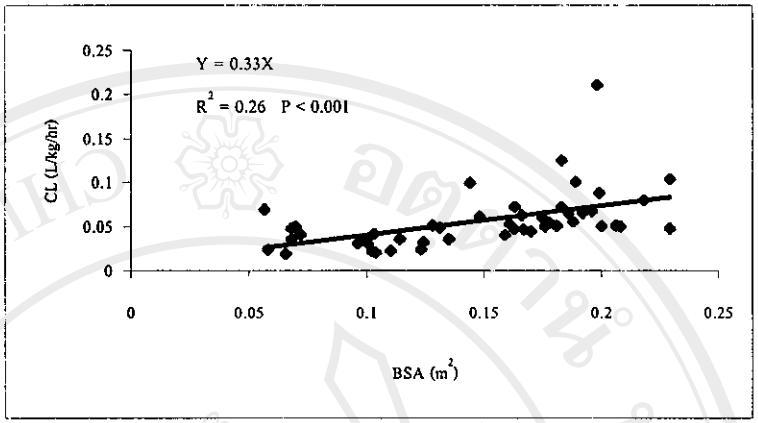

Figure 23. Correlation between BSAand CL.

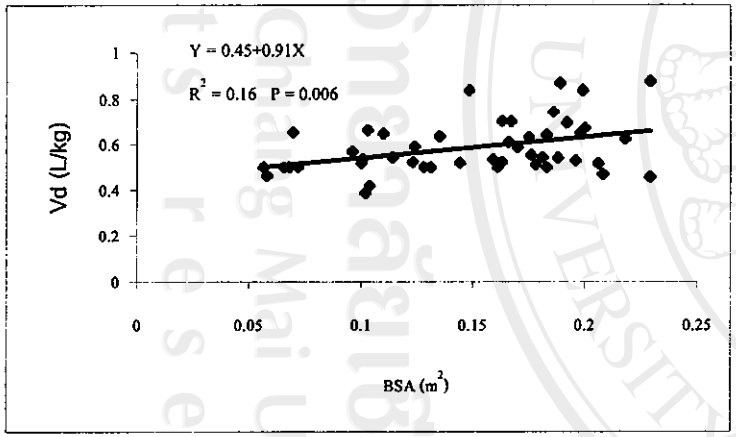

Figure 24. Correlation between BSA and V_d.

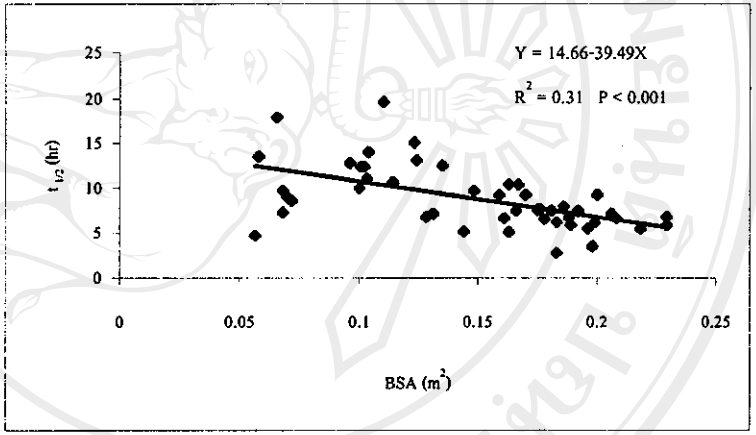

Figure 25. Correlation between BSA and $t_{1/2}$.

Table 23. Serum creatinine and BUN concentrations at the first, third and sixth dose in each gestational age group.

Dose	Gestational age							
	≤ 29 weeks		30-33 weeks		34-37 weeks		≥ 38 weeks	
	Serum creatinine (mg/dl)	BUN (mg/dl)	Serum creatinine (mg/dl)	BUN (mg/dl)	Serum creatinine (mg/dl)	BUN (mg/dl)	Serum creatinine (mg/dl)	BUN (mg/dl)
First dose	1.02 ± 0.18 (0.8-1.3)	17.44 ± 5.72 (11.0-28.0)	0.98 ± 0.29 (0.7-1.6)	14.70 ± 5.92 (8.0-23.0)	0.87 ± 0.13[*,†] (0.7-1.1)	11.93 ± 3.56 (6.0-20.0)	0.92 ± 0.36[*,†] (0.14-1.8)	13.56 ± 6.58[†] (7.0-29.0)
Third dose	1.00 ± 0.17 (0.7-1.3)	25.86 ± 14.18 (8.0-47.0)	0.76 ± 0.18 (0.5-1.1)	17.43 ± 6.83 (10.0-30.0)	0.47 ± 0.20 (0.2-0.8)	10.15 ± 5.18 (5.0-26.0)	0.52 ± 0.20 (0.2-0.9)	10.5 ± 6.62[†] (5.0-32.0)
Sixth dose	-	-	-	-	0.48 ± 0.18 (0.3-0.7)	8.40 ± 3.21 (5.0-13.0)	0.47 ± 0.11 (0.3-0.9)	6.27 ± 2.49 (3.0-11.0)

Present as mean ± SD and range

Normal range of serum creatinine in neonate = 0.34-0.60 mg/dl

Normal range of BUN in neonate = 12.9-25.8 mg/dl

Paired t test within group; the mean difference is significant at $P<0.05$

[*] Significant difference from third dose

[†] Significant difference from sixth dose

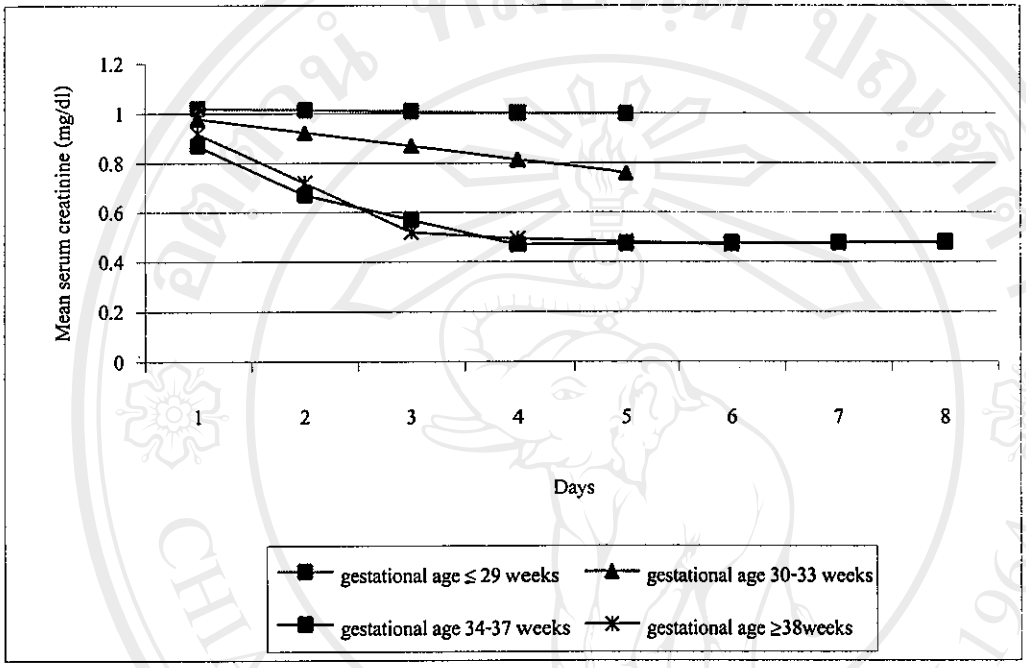

Figure 26. Mean serum creatinine level in each gestational age group.

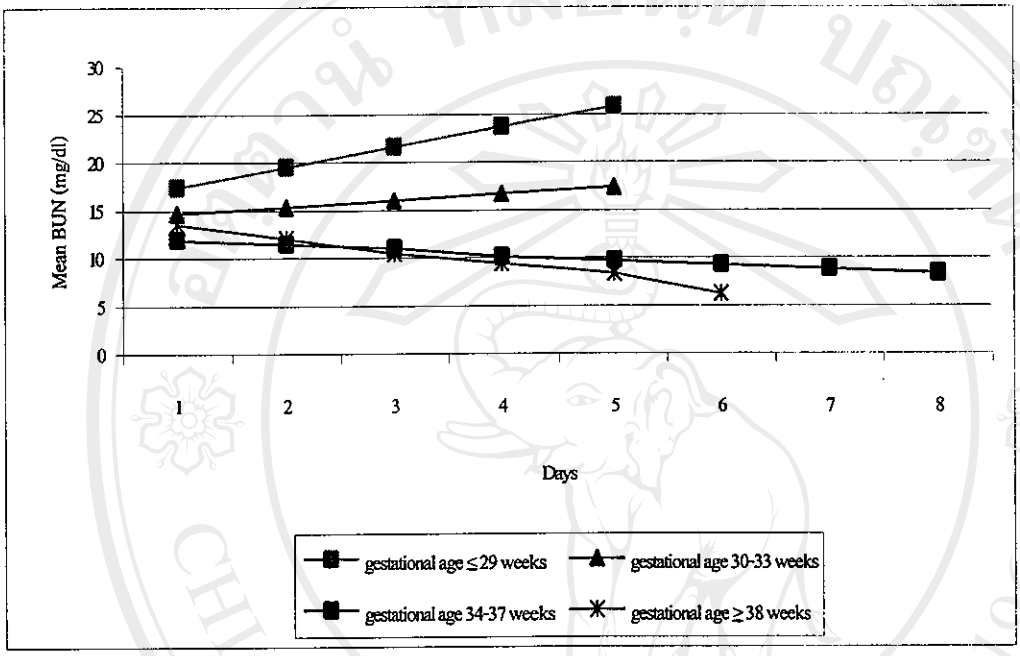

Figure 27. Mean BUN level in each gestational age group.