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# Preterm Birth in Taiwan

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# Preterm Birth in Taiwan

## Introduction

Despite progress in maternal-fetal medicine, preterm birth is still one of the most complicated problems in modern obstetrics. Preterm birth is responsible for two thirds of neonatal deaths in the United States and 85% of early neonatal deaths not due to lethal congenital deformities in England.[1] The incidence of preterm birth lies between 5 and 10 per cent of all births in developed countries. The incidence of preterm births in Taiwan has not been formally reported. However, neonatal death due to certain conditions originating in the perinatal period was the leading cause of death in children under one year of age in Taiwan in 1994.[2] In addition to survival, another important issue is the quality of life achieved by quite immature, extremely-low-birthweight infants. It is apparent that appreciable compromise, both physical and intellectual, afflicts many of these children. The dollar cost of caring for these children is one measure of the national burden of prematurity.

Refinements in neonatal care have improved the outcome for some neonates. Improve nutrition, awareness of prenatal care and pathophysiology of low-birthweight neonates, the development of neonatal care units, the skillful use of respirators, and improvements in laboratory tests have made it possible to significantly reduce the low-birthweight neonatal mortality rate. The neonatal mortality rate in Taiwan has decreased from 17.79% in 1956 to 1.74% in 1987[3].

To develop a database for Taiwan, we collected and analyzed data on preterm deliveries from 1987 to 1996 from six hospitals. From these and a review of the literature, we discuss the epidemiology of this problem and explore possible strategies for the prevention of preterm birth and some of its consequences.

## Epidemiology

### Incidence

To determine the nature of preterm birth in Taiwan, we reviewed the birth records from 1987 and 1996 at six hospitals. These six hospitals were Tzu-Chi Hospital in Hualien, and Veterans General Hospital, Chang Gung Memorial Hospital, Tri-Service General Hospital, Taipei Municipal Women and Children's Hospital, and Mackay Memorial Hospital all in Taipei. (Table 1) The definition of preterm birth was any delivery, regardless of birth weight, that occurred before 37 completed weeks from the first day of the last menstrual period. (American College of Obstetricians and Gynecologists, 1995) Of a total of 142,303 deliveries, there were 10,890 preterm births. The incidence of preterm birth was 7.65%. The annual incidence was from 4.63% in 1987, 5.40% in 1988, 5.66% in 1989, 5.51% in 1990, 6.19% in 1991, 8.68% in 1992, 8.49% in 1993, 8.93% in 1994, 8.97% in 1995, to 10.17% in 1996. (Figure 1) It appeared to increase year by year. However, the preterm delivery rate varies from institution to institution and not all hospitals showed an increased rate. (Figure 2) Mackay Memorial Hospital's 1992-1996 data was used in this report and its higher preterm delivery rate (10.66% ~14.54%)

may have elevated the total preterm delivery incidence for those years.

## Gestational age and birthweight distribution of preterm infants

Figure 3 shows the gestational age distribution of preterm infants in these 6 hospitals. The delivery rate for infants between 20 and 28 weeks was under 0.2% per week. A gestational age between 34 and 36 weeks was most frequently seen. Of all preterm births 0.94% were delivered at 34 weeks of gestation, 1.34% at 35 weeks of gestation, and 2.42% at 36 weeks.

The birth weight distribution of the preterm infants is shown in Figure 4. Very-low-birthweight (VLBW) premature babies ( <1500gm ) comprised 24.80% of all preterm births. Low-birth-weight infants (LBW), excluding VLBW premature babies-i.e. babies weighing between 1500gm and 2500gm, were 41.39% of all preterm births. About 0.36% of preterm infants weighed more than 4000gm. Some were actually preterm births, but in some the gestational age might have been miscalculated. VLBW infants were 1.94%, and LBW infants 3.24% of all births. A total of 5.18% of premature babies had a birthweight less than 2500gm. Kessel and colleagues[4] documented that the delivery rate of premature babies under 2500gm decreased from 3.81% in 1970 to 3.54% in 1980 in United States. Our rates were higher. Soong and colleagues[5] reported the incidence of low-birthweight infants ( $\leq$ 2500g ) was 8.1% at Veterans General Hospital in Taipei between 1987 and 1989. Yan et al[6] showed an increase in the incidence of LBW babies from 4.1% in 1979-1982 to 7.6% in 1990-1992. However, the latter two both included all LBW infants, both LBW premature babies and LBW term babies.

## Clinical characteristics

Of the total of 10,890 preterm births, 4.95% of mothers were under 20 years of age and 17.36% were older than 35. 43.96% of cases were primipara, 37.9% were second parity, 12.66% were third parity, and 5.46% was forth parity. Regarding to modes of delivery, there were 58.87% vaginal delivery, and other 41.13% cesarean section (Table 1). The ratio of male to female was 1.16.

There were 5,288 deliveries at Mackay Memorial Hospital (MMH) in Taipei in 1995, of which 1.79% were mothers under 20 years of age and 11.12% were older mothers. This was significantly different than the overall data in this report. The male-female ratio at MMH was 1.12, similar to the overall ratio of 1.16. According to the annual report of Taiwan Society of Perinatalogy in 1996, the cesarean rate was about 35%. However, the present study showed a higher cesarean rate for preterm births (41.13%). This may be due to a higher rate of obstetric complications with preterm births. In order to better the perinatal outcome and because of fears of medico-legal action against obstetricians for delivery of neurologically abnormal infants, clinicians often perform cesarean sections. In addition, advances in neonatology have made it possible to salve more premature infants, and obstetricians can therefore to manage preterm births more aggressively. In recent reports, however, it is difficult to attribute solely the increased cesarean rate makes the low perinatal mortality rate.[7]

## Multiple pregnancy and preterm birth

According the annual report of Taiwan Society of Perinatalogy in 1996, multifetal pregnancies had a higher rate of preterm deliveries. The frequency of preterm births was 75% and 36.9%, respectively, for triplets and twins, compared to 5.6% for singletons. The average period of gestation was about 39.2, 36.5, and 32.6, respectively, for singletons, twins, and triplets. Similar results were shown in our report. The frequency in our study was 7.0%, 69.3%, 87.0%, and 100%, respectively, for singletons, twins, triplets, and quadruplets. This showed that the higher the number of fetuses, the higher the frequency of preterm birth. With the recent use of selective fetal reduction, the fetal number can be decreased to improve the perinatal outcome in multiple pregnancy.

## Obstetric factors

Some peri-delivery diagnoses either at admission or discharge are related to preterm birth. Table 2 shows these diagnoses. The cause of preterm birth in 40.6% was unknown. The most commonly identified cause was preterm premature rupture of membranes (PPROM; 20.8%), followed by antepartum hemorrhage (9.74%). In cases with antepartum hemorrhage, 6.6% were due to placenta previa, and 3.08% due to placental abruption. Altogether, 9.21% of cases had preeclampsia, 7.25% diabetes, 5.86% fetal anomaly, 3.30% cervical incompetence, 1.77% uterine anomaly, 1.86% chorioamnionitis, and 0.62% trauma or surgery. A wide spectrum of causes and demographic factors have been implicated in the birth of preterm infants. Lettieri and colleagues[8] (1993) analyzed 50 consecutive preterm births and identified conditions sufficient to explain 96 percent. Approximately half were indicated deliveries due to placenta previa or abruption. Amniotic fluid infections comprised 38%, immunological factors 30%, cervical incompetence 16%, uterine anomaly 14%, maternal complications (e.g. preeclampsia, drug intoxication) 10%, trauma or surgery 8%, fetal anomalies 6%, and 4% showed no cause. More than half of the pregnancies resulting in preterm birth had two or more possible causes, suggesting that many such births are multifactorial in origin. The difference in our study may be due to the retrospective nature of our study. It was difficult to get more detailed and uniform data and there were more variables in methodology. However, race and lifestyle factors should be also considered.

# Perinatal and maternal mortality

## Perinatal mortality

The perinatal mortality rate of preterm infants was 10.52%. For infants born between 20 and 32 weeks of gestation, the perinatal mortality rate increased to 27.4%. The perinatal mortality rates for preterm births in multifetal pregnancy were 10.68%, 7.30%, 9.06%, and 6.82%, respectively, for singletons, twins, triplets and quadruplets. The rates were not elevated

with the fetal number.

## Maternal mortality

Maternal mortality in Taiwan has decreased from 196.56 in 1952, and 32.35 in 1974 to 9.85 per 100,000 live births in 1985. In this report, there were 15 maternal deaths in a total of 10,890 preterm births at the six hospitals. The maternal mortality was 1.38 per 1,000 live births. The higher rate can be attributed to the fact that these six hospitals are all secondary or tertiary medical centers in Taiwan, with facilities for handling high-risk pregnancies, and preterm births may frequently be associated with more serious obstetric complications.

## Neonatal mortality of preterm infants

Some very small infants do survive when provided with prolonged, very expensive intensive care. This has created serious problems in decision making. The significant morbidity in these tiny infants can affect each organ and system, including neonatal respiratory distress syndrome, interstitial emphysema, patent ductus arteriosus, apnea, intraventricular hemorrhage, hypothermia, necrotizing enterocolitis, feeding problems, and abnormal metabolism in glucose, bilirubin, and calcium. In this study, 13.53% of preterm infants required neonatal intensive care unit (NICU) care.

Other key issues include the rates of neonatal mortality and morbidity. From NICU data at Mackay Memorial Hospital in Taipei, the 1996 neonatal survival rates according to gestational age are shown in Table 3. There were no survivors among babies delivered before 22 weeks of gestation. Infants delivered at 28 weeks of gestation had a survival rate of 75% and 95% can be achieved in babies who were delivered after 31 weeks of gestation.

According to the birth weight table (Table 4), there were no survivors with a birthweight less than 500gm. Preterm infants with a birthweight 801-900gm had a survival rate of 71%, and those 901-1000gm had a survivor rate of 89%. More than 90% with a birthweight greater than 1500gm survived. Preterm infants with a birthweight 1500-2500gm had a survival rate of 90-100%, and those heavier than 2500gm had a 92.5% survival rate. This has significantly elevated over past years. Figure 5 shows the survival rates of infants weighing less than 1000 gm in the NICU of Mackay Memorial Hospital from 1993 to 1996. In general, it demonstrates that survival rates have increased. Lin and colleagues also reported a study of very-low birthweight infants at Mackay Memorial Hospital in 1987.[9] The survival rate was zero in infants with a birthweight 500-799gm, 46% for those 800-999gm, 83% for those 1000-1249gm, and 81% for those 1250-1500gm. The main cause of infant death was intracranial hemorrhage (55%), followed by hyaline membrane disease and its complications (32%). Similar results were documented by pediatricians at National Taiwan University Hospital. The neonatal survival rate had also elevated significantly. A rate of 97% can be achieved in babies with birthweight larger than 1500gm. Premature babies with a birthweight less than 1500gm had an increased survival rate from 83% in 1991 to 94% in 1996. In infants less than 1000gm, the survival rate increased

from 43% in 1991 to 60 to 70% in 1996.

# Discussions

The pathophysiology of preterm birth is still unclear. The mechanism of treatment is, thereafter, unknown and it is not only difficult not only to cure but also to prevent effectively. Preterm birth rates have remained unchanged (about 5-10%) in United States over the past decades. It appears that the rate varies from country to country and institution to institution. In this study, we also noted the incidence varied from institution to institution. The six hospitals are all secondary or tertiary medical centers, with facilities for handling high-risk pregnancies. These institutions may therefore have a higher percentage of preterm birth than that of the general population. Thus, the estimated incidence in this report may be slightly higher than the Taiwan population at large. With advances in assisted reproductive technology, the incidence of multifetal pregnancies has increased markedly. This may also have increased preterm births.

How can we reduce the incidence of preterm birth? Possible causes of preterm labor include infection of the vagina and cervix, cervical incompetence, uterine anomaly, overdistension of the uterus, maternal complications, fetal distress, and hypersensitivity to oxytocin. In only 25% of cases can a definite cause be found. Therefore, it is difficult to develop effective methods to prevent preterm birth. The successful prospective identification of a subgroup of pregnancies at significantly increased risk of preterm labor and delivery allows the rational use of interventions aimed at prolonging gestation, be they psychological, social or pharmacological. In an effort to provide a useful screening test for preterm delivery risk, several scoring systems have evolved that quantify a variety of epidemiological and pregnancy features, digital assessment of the cervix. The scoring system described by Creasy et al (1980) [10], consisted of 37 risk factors. If the patient's score was higher than 10, she was classified as high risk. Holbrook et al (1989) simplified this system[11], but kept the effectiveness. His system classified 14.1% of women as high risk. The sensitivity was 41%, and the positive predictive value was only 24.6%. Patients who had one major factor or two minor factors were classified as high risk. The 12 major factors were multiple pregnancy, prior preterm delivery, prior preterm labor but term delivery, abdominal surgery during pregnancy, DES exposure, polyhydramnios, uterine anomaly, prior cervical conization, prior admission due to suspected preterm labor, dilatation of the cervix greater than 1cm at 32 weeks of gestation, effacement of the cervix more than 50% at 32 weeks of gestation, and history of more than one mid-trimester abortion. The six minor factors included febrile disease during pregnancy, vaginal bleeding after 12 weeks of gestation, history of renal disease, smoking more than 10 cigarettes per day, history of one mid-trimester abortion, and history of more than two early trimester abortions. However, the limitations of performance and potential disadvantages means that formal risk scoring for preterm birth lacks many of the characteristics required of effective screening tests. Alternative methods, such as detecting fetal fibronectin in cervico-vaginal secretions[12], measuring cervical length by ultrasound[13], and evaluating preterm uterine activity at home[14], have been and

are currently being explored, but appear largely ineffective at present.

Preterm birth is not always or even usually the result of spontaneous preterm labor. Women at risk for preterm delivery may present initially in a variety of ways. The clinical circumstances or "proximate causes" of preterm birth may vary in different patient groups. In our study, most patients had uncomplicated preterm births. The proportion of patients presenting with preterm labor, preterm rupture of membranes (PROM), or medical complications was equivalent in the report by Romero et al.[15] (Table 5). Meis and colleagues[16] analyzed the causes of delivery before 37 weeks in 1134 live infants delivered in North Carolina by income group. Women obtaining private care were more likely to present with uncomplicated preterm labor. Women on public assistance more often presented with PROM. It appears that more uncomplicated preterm labor in Taiwan is due to the improvement in the economy, advances in public health, and better perinatal care programs. However, this needs further study.

Another important issue is how we can increase the neonatal survival rate. Advances in neonatal medicine have served considerably to improve the outcome for the premature baby. Progress in medicine, the development of neonatal intensive care centers, and use of new techniques have made it possible to further increase the neonatal survival rate. However, a review of the literature concerning low-birthweight infants in Taiwan, [3,9,17,18,19] shows that babies referred from one hospital to another have a higher mortality rate. The reason is lack of an effective emergency medical transport system in Taiwan. If women with a high risk of preterm birth can be referred early to hospitals with a well-developed NICU, which is associated with better quality of prenatal and perinatal care, the neonatal survival rate of low-birthweight infants may increase.

Because of the increasing neonatal survival rate, more premature babies are delivered before complete maturation of organs and systems. Many are still subject to long-term sensorineural, growth and respiratory problems. Aside from aggressive preventive programs, obstetric management in preterm labor is relatively important. The present initial obstetric management of the patient with preterm labor should be administration of a tocolytic agent. However, prophylactic use of tocolytic agents is not effective in neither prolonging gestational age nor mean birthweight of preterm infants.[20] The use of ultrasound in measuring residual amniotic fluid volume, and evaluating effacement and length of cervix can provide effective assessment in the management of preterm birth with PPROM.[21] However, the prophylactic use of antibiotics, tocolytic agents, and glucocorticoids, culture and prevention of β-group streptococcus, and ideal modes of delivery have been debated for decades. In general, gestational age and birth weights are the key elements in neonatal survivals. Preventing perinatal infection and providing good neonatal resuscitation can reduce neonatal sequelae.[22]。

Preterm labor and delivery remain a major cause of perinatal morbidity, mortality and long-term adverse neurodevelopmental outcome in Taiwan. There are still many unknown issues in preterm birth. Maternal anxiety, discomfort, and society and family problems caused by preterm babies need to be addressed. Understanding the etiology of preterm birth may improve efforts at its prevention and treatment. We have tried to provide information related to preterm birth in Taiwan. However, a retrospective study is not

enough to increase our understanding. To provide more detailed information, further larger, prospective studies are needed. ◦

1. **Table 1. Preterm births at six hospitals in Taiwan from 1987 to 1996**

| | TCH | VGH | TSH | CGH | WCH | MMH | Total |
|---|---|---|---|---|---|---|---|
| Years | 1987-96 | 1987-96 | 1992-96 | 1990-96* | 1987-96† | 1992-96 | |
| Total deliveries | 7119 | 27106 | 7648 | 26075 | 46672 | 27683 | 142303 |
| Singleton | 6994 | 26852 | 7541 | 25704 | 46365 | 27395 | 140851 (98.9%) |
| Twins | 122 | 219 | 103 | 352 | 296 | 259 | 1351 (0.95%) |
| Triplets | 3 | 33 | 4 | 17 | 8 | 28 | 93 (0.065%) |
| Quadruplets | 0 | 2 | 0 | 2 | 3 | 1 | 8 (0.0056%) |
| Total PD | 549 | 2550 | 537 | 1917 | 2144 | 3193 | 10890 (7.65%) |
| Maternal age <20 | 47 | 198 | 10 | 22 | 113 | 149 | 539 (4.95%) |
| Maternal age≥35 | 56 | 499 | 113 | 367 | 286 | 570 | 1891 (17.36%) |
| Parity | | | | | | | |
| 1 | 214 | 998 | 268 | 921 | 933 | 1453 | 4787 (43.96%) |
| 2 | 192 | 861 | 208 | 734 | 833 | 1299 | 4127 (37.90%) |
| 3 | 99 | 515 | 51 | 213 | 298 | 203 | 1379 (12.66%) |
| ≥4 | 44 | 176 | 8 | 47 | 80 | 238 | 595 (5.46%) |
| C/S rate | 42.99% | 45% | 37.33% | 49.31% | 30.68% | 40.66% | 41.13% |
| PD of singleton | 474 | 2240 | 493 | 1742 | 1996 | 2923 | 9868 |
| PD of twins | 72 | 279 | 41 | 161 | 138 | 245 | 938 |
| PD of triplets | 3 | 29 | 3 | 12 | 7 | 24 | 78 |
| PD of quadruplets | 0 | 2 | 0 | 2 | 3 | 1 | 8 |

TCH = Tzu-Chi Hospital in Hualien, VGH = Veterans General Hospital in Taipei, CGH = Chang Gung Memorial Hospital in Taipei, TSH = Tri-Service General Hospital, WCH = Taipei Municipal Women and Children's Hospital, MMH = Mackay Memorial Hospital in Taipei, PD= preterm deliveries, C/S = cesarean section.

* The data from CGH in 1990 included only July to December.

† The data from WCH in 1987 and 1996 both included January to June.

**Table 2. Obstetric factors**

| | TCH *N* | VGH *N* | TSH *N* | CGH *N* | WCH *N* | MMH *N* | Total % |
|---|---|---|---|---|---|---|---|
| PPROM | 56 | 626 | 80 | 304 | 102 | 1024 | 20.8 |
| Preeclampsia | 55 | 390 | 45 | 156 | 39 | 295 | 9.21 |
| DM | 7 | 612 | 8 | 92 | 15 | 24 | 7.25 |
| Placenta previa | 5 | 256 | 28 | 75 | 63 | 249 | 6.6 |
| Fetal anomaly | 38 | 161 | 40 | 194 | 56 | 129 | 5.86 |
| Cervical incompetence | 3 | 194 | 4 | 27 | 2 | - | 3.30 |
| Placenta abruption | 22 | 106 | 16 | 109 | 16 | 63 | 3.08 |
| Chorioamnionitis | 0 | 34 | 5 | 78 | 12 | - | 1.86 |
| Uterine anomaly | 1 | 171 | 4 | 6 | 4 | 0 | 1.77 |
| Trauma or surgery | 3 | 17 | 0 | - | 4 | 26 | 0.62 |
| Unknown | 397 | 98 | 353 | - | 495 | 1721 | 40.6 |

PPROM = preterm premature rupture of membranes, DM = diabetes mellitus.

-: No data

**Table 3. Survival rates of preterm livebirths as a function of gestational age from the NICU of Mackay Memorial Hospital in 1996.**

| Gestational age (wk.) | Survival rates | | |
|---|---|---|---|
| | Survivor | Total cases | % |
| ≤ 23 | 1 | 10 | 10% |
| 24 | 2 | 9 | 22% |
| 25 | 6 | 7 | 86% |
| 26 | 14 | 25 | 56% |
| 27 | 17 | 24 | 71% |
| 28 | 25 | 33 | 76% |
| 29 | 25 | 30 | 83% |
| 30 | 35 | 36 | 97% |
| 31 | 36 | 42 | 86% |
| 32 | 56 | 58 | 97% |
| 33 | 65 | 69 | 94% |
| 34 | 55 | 57 | 96% |
| 35 | 57 | 60 | 95% |
| 36 | 78 | 80 | 97.5% |

**Table 4. Survival rates of preterm livebirths as a function of birthweight from the NICU of Mackay Memorial Hospital in 1996.**

| Birthweight (gm) | Survival rates | | |
|---|---|---|---|
| | Survivor | Total cases | % |
| ≤500 | 0 | 7 | 0 |
| 501-600 | 1 | 6 | 17% |
| 601-700 | 1 | 7 | 14% |
| 701-800 | 5 | 11 | 45% |
| 801-900 | 10 | 14 | 71% |
| 901-1000 | 16 | 18 | 89% |
| 1001-1100 | 14 | 18 | 78% |
| 1101-1200 | 18 | 23 | 78% |
| 1201-1300 | 21 | 26 | 81% |
| 1301-1400 | 24 | 28 | 86% |
| 1401-1500 | 29 | 31 | 94% |
| 1501-1600 | 27 | 30 | 90% |
| 1601-1700 | 36 | 38 | 95% |
| 1701-1800 | 29 | 31 | 94% |
| 1801-1900 | 19 | 19 | 100% |
| 1901-2000 | 25 | 27 | 93% |
| 2001-2100 | 34 | 35 | 97% |
| 2101-2200 | 31 | 31 | 100% |
| 2201-2300 | 34 | 38 | 89% |
| 2301-2400 | 22 | 23 | 96% |
| 2401-2500 | 49 | 51 | 96% |
| ≥2500 | 395 | 427 | 93% |

**Table 5. Proximate causes of preterm birth**

| Romero et al, 1989<br>New Haven, Connecticut | Meis et al, 1987<br>North Carolina | |
|---|---|---|
| | Public Assistance | Private |
| 1/3 Preterm labor | 34% Preterm labor | 55% Preterm labor |
| 1/3 Preterm PROM | 46% Preterm PROM | 27% Preterm PROM |
| 1/3 Maternal or fetal complication | 20% Medical complication | 18% Medical complication |

**Figure 1. Annual incidence of preterm births in six hospitals in Taiwan from 1987 to 1996.**

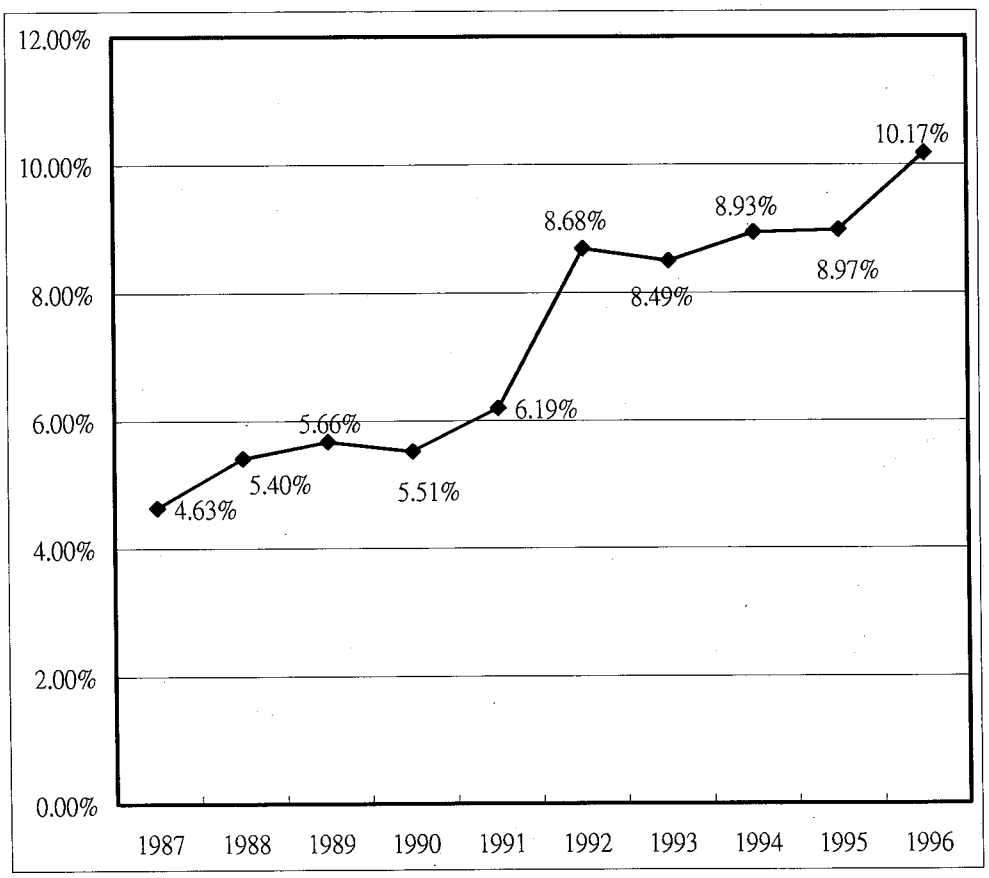


**Figure 2. Annual preterm delivery rate in six hospitals in Taiwan from 1987 to 1996**

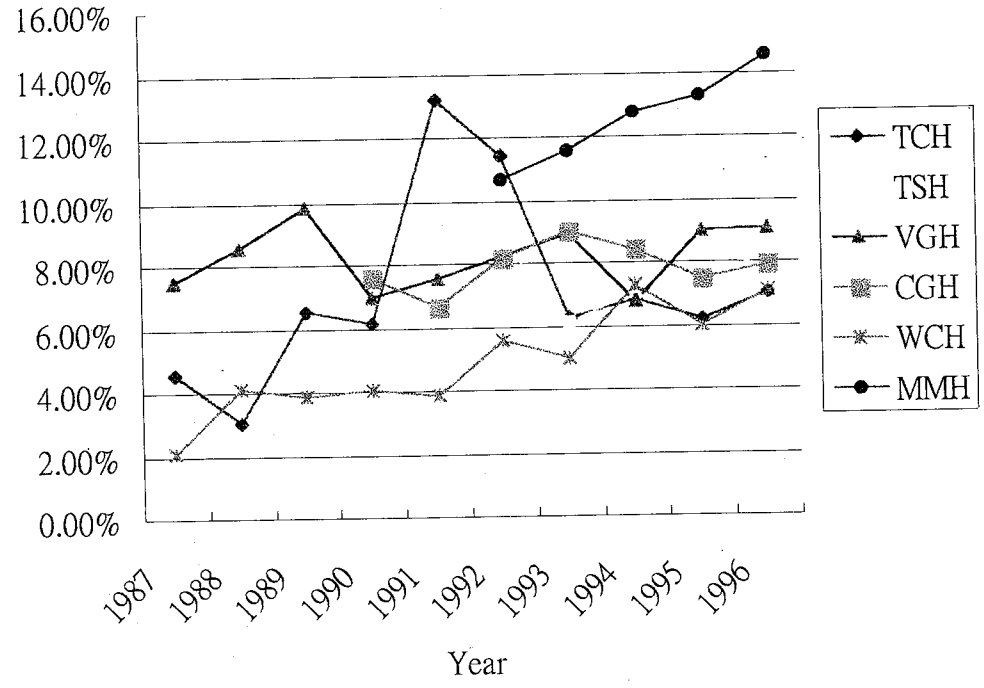



**Figure 3.Gestational age distribution of preterm infants**

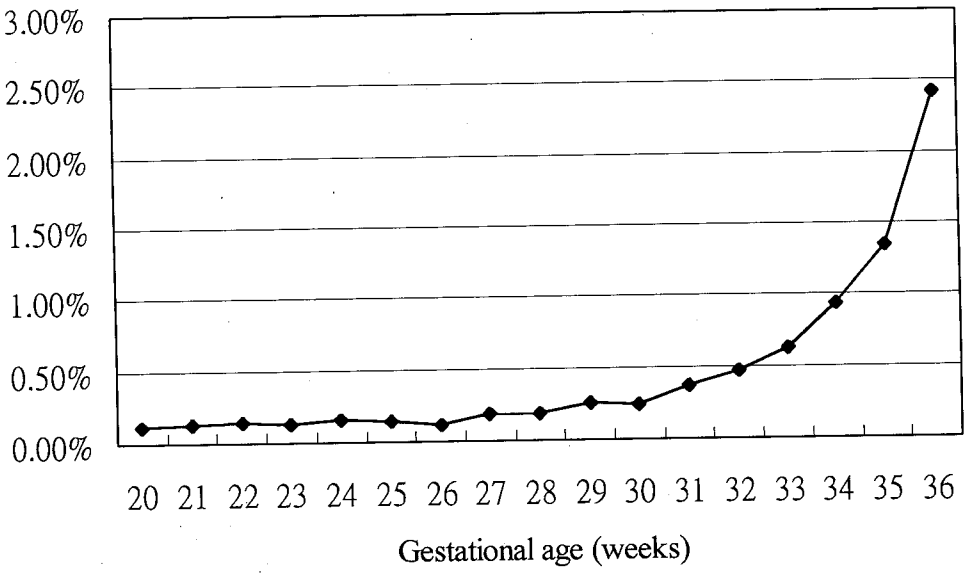


**Figure 4. Birthweight distribution of preterm infants**

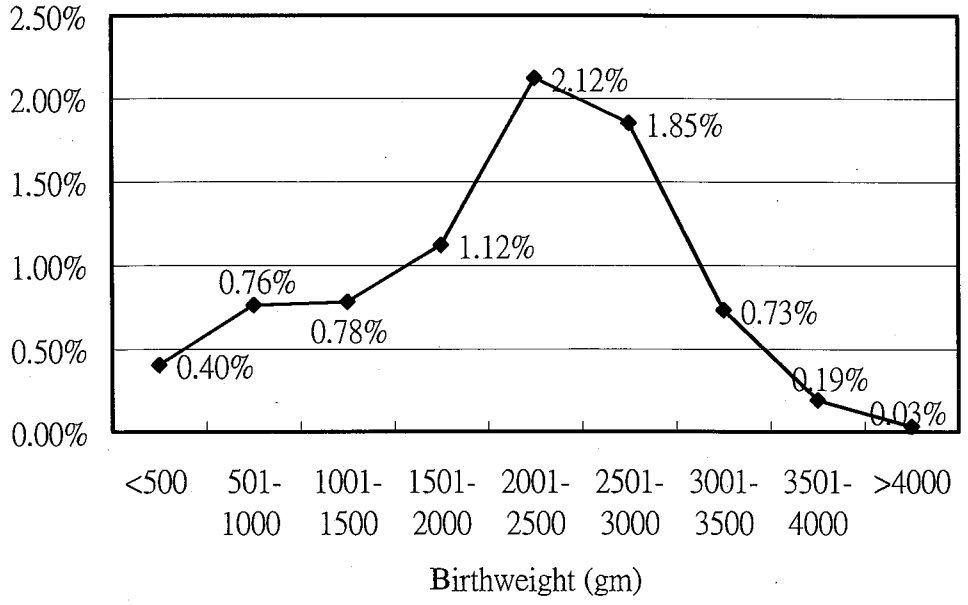
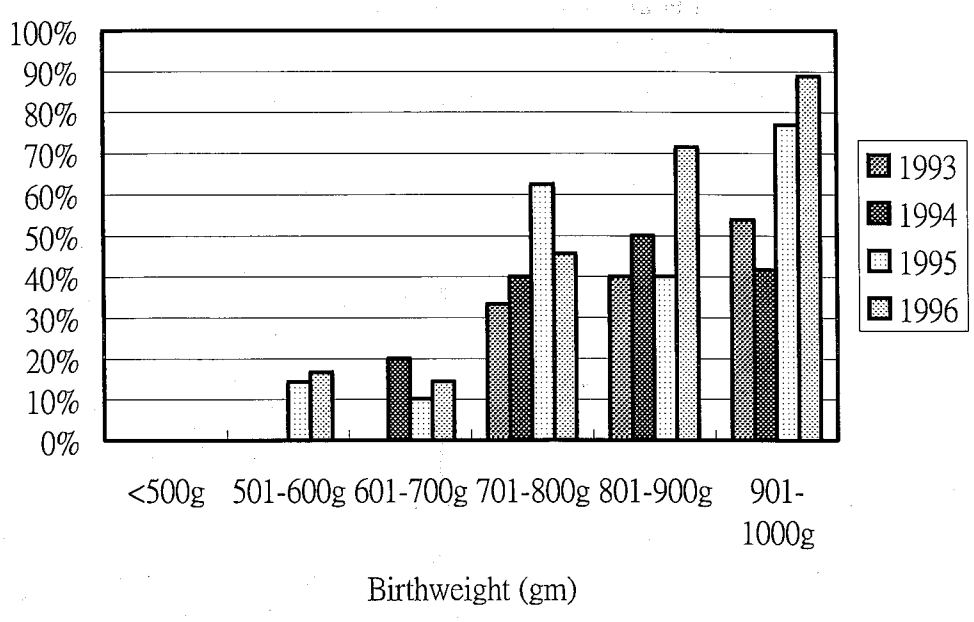



**Figure 5. Survival rates in infants with birthweight < 1000gm in the NICU of Mackay Memorial Hospital from 1993 to 1996.**



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# 台灣之早產

## 前　言

儘管目前產科學的進步，早產仍是現代產科學中最複雜的課題之一。在美國，有三分之二的新生兒死亡即肇因於此；倘若除去嚴重致死性之先天性畸型，在英國有 85%的新生兒死亡是源於早產[1]。通常早產的發生率介於 5-10%之間，目前國內並沒有官方正式的統計數據，不過，根據台灣省婦幼衛生研究所在 1996 年所發表的資料，源於周產期病態之新生兒死亡高居 1994 年台灣地區零歲幼兒十大死因之第一位[2]。此外，由早產伴隨的新生兒急慢性問題也相當多，不僅會造成新生兒罹病，早產兒的照顧費用亦非常可觀，如無醫療保險，也可能造成另一種社會問題。

值得慶幸的是，由於目前新生兒學在小兒科的領域發展迅速，尤其近年來由於營養的改善，對胎兒產前照顧及低出生體重兒生理病理的瞭解，新生兒加護病房的設立，呼吸器的改良及使用技術臻於成熟，檢驗技巧的改良等，使得低出生體重兒的死亡率顯著降低。台灣地區新生兒死亡率已從 1956 年的 17.79%降低到 1987 年的 1.74%[3]。

為建立本土的資料庫，我們分析由 1987-1996 年間國內六家大型醫院早產的相關數據，並參考國內外文獻，來探討國內早產的發生與照護。

## 流行病學

### 發生率

經由回溯性統計台灣地區六家大型醫院，從 1987 到 1996 年的十年間，其生產及早產登錄之相關資料，這六家大型醫院包括花蓮慈濟醫院、台北榮民總醫院、台北長庚紀念醫院、台北三軍總醫院、台北市立婦幼醫院、台北馬偕紀念醫院（表 1）。早發性生產的定義是根據 1995 年美國婦產科學院所提出的：懷孕 20 週之後、37 週之前的生產（114 至 259 天之間），而不論胎兒之出生體重。在總計共 142,303 產次生產中，其中有

10,890 產次的早發性生產，發生率為 7.65%；每年的早產發生率則由 1987 年的 4.63%、1988 年的 5.40%、1989 年的 5.66%、1990 年的 5.51%、1991 年的 6.19%、1992 年的 8.68%、1993 年的 8.49%、1994 年的 8.93%、1995 年的 8.97%、到 1996 年的 10.17%不等（如圖 1）。發生率看似逐年增加，但若就各單一醫院的逐年早產發生率而言，則並非所有的醫院均有如此的趨勢(如圖 2)，而馬偕醫院由於有較高的早產發生率(10.66%~14.54%)，因此從 1992 年起由於馬偕醫院的加入統計，使得早產發生率可能因此攀高。

## 早產妊娠週數與出生體重分佈

若以妊娠週數來分別探討各個週數的早產發生率，我們可以得到如圖 3 之分佈圖，其中妊娠二十至二十八週的各妊娠週數之早產均各約佔所有生產的 0.2%以下，而三十四到三十六週的早產則最為常見，分別是 34 週的佔所有生產的 0.94%，35 週的 1.34%，及 36 週的 2.42%；此外，新生兒存活率較低且罹病率較高的妊娠二十至三十二週之早產共佔所有生產的 2.62%。

若以出生體重來看的話，則可得如圖 4 之分佈圖。其中極低出生體重兒（<1500g）約佔所有早產兒的 24.80%，低出生體重兒（但不含極低出生體重兒，即 1500g≤BW<2500g）約佔 41.39%。另外有 0.36%的早產兒其出生體重大於 4000g，其中部分真的是早產，而有些則可能為妊娠週數計算錯誤所致。此外，若以所有活產來看，極低出生體重早產兒約佔 1.94%，而低出生體重早產兒則佔 3.24%。這樣的結果與 Kessel 等人報告[4]在美國 1970 年至 1980 年間，低出生體重早產兒（≤ 2500g）由 3.81%降到 3.54%的結果相比較，我們的發生率還是較高。而台北榮民總醫院的 Soong 等人則報告[5]，在 1987 年到 1989 年間來低出生體重兒（≤ 2500g）約佔所有活產的 8.1%；此外，台北三軍總醫院的 Yan 等人也報告[6]低出生體重兒的發生率，由 1979-1982 年的 4.1%增加到 1990-1992 年的 7.6%。不過，後面這二者均為所有低出生體重兒的發生率，其中包含了低出生體重早產兒及低出生體重足月兒。

## 生產特徵

在這 10,890 產次早產中，未滿 20 歲的產婦佔 4.95%，而高齡產婦（35 歲以上）則佔 17.36%；就產婦胎次而言，首次生產的佔 43.96%，第二胎的佔 37.90%，第三胎的佔 12.66%，第四胎以上的佔 5.46%；至於生產方式，經陰道生產的佔 58.87%，剖腹生產的佔 41.13%（表 1）。此外，男性與女性早產兒的比例約為 1.16。

以上早發性生產特徵與台北馬偕紀念醫院 1995 年全年所有 5,288 產次相比較，在產婦年齡方面，馬偕醫院未滿 20 歲的產婦共佔 1.79%，而高齡產婦則佔 11.12%，均有顯著差異；在男女比例方面，馬偕醫院為 1.12，並沒有顯著差異；在剖腹產比例方面，根據中華民國周產期醫學會一九九六年關於台灣剖腹產之工作報告中，目前台灣之剖腹產率約為 35%，早產的剖腹產率在此為 41.13%，有顯著的提升。其中部分是因為早產常合併有其他產科併發症，為求較好的周產期結果，同時避免醫療糾紛，而施行剖腹產；此外，現代新生兒科的進展，使得早產兒的存活率大增，也使得產科醫師採取更積極的處置，來保障母體和胎兒的安全，這些因素均可能造成上升的剖腹產率。不過目前研究顯示，早產兒死亡率的降低，很難單純歸因於剖腹產率的升高。[7]

## 多胞胎與早產

在中華民國周產期醫學會 1996 年工作報告中，多胞胎妊娠發生早產的機率較大，三胞胎與雙胞胎妊娠發生早產的機率分別為 75%與 36.9%，而單胞胎則只有 5.6%；單胞胎的平均妊娠期為 39.2 週，雙胞胎與三胞胎則為 36.5 週與 32.6 週。在我們的統計中也有這種現象，單胞胎、雙胞胎、三胞胎與四胞胎妊娠的早產發生率分別為 7.0%、69.3%、87.0%及 100%，可見多胞胎的胎兒數目愈多，早產的機率愈大。近幾年來由於減胎術的施行，能有效的降低子宮內胎兒的數目，因而減少因多胞胎早產所致之周產期預後不良。

## 產科因素

一些生產前後的診斷可能與早產有關，因此在表 2 便統計早產生產前後之診斷。其中最多的是找不到病因的，約佔 40.6%；其次是產前早期破水，約佔 20.8%；產前出血則佔 9.74%，其中前置胎盤佔 6.6%，胎盤早期剝離佔 3.08%；子癇前症也佔 9.21%；糖尿病佔 7.25%；胎兒異常佔 5.86%；子宮頸閉鎖不全佔 3.30%；子宮異常佔 1.77%；絨毛羊膜炎佔 1.86%；因傷害或手術所致的則佔 0.62%。事實上，有些早產的病例並不僅只有一個原因，而是有多重致病因素的。我們與 Lettieri 在 1993 年所發表的早產致病因素之統計相比較 [8]，在他們的統計中，前置胎盤及胎盤早期剝離佔 50%，羊水感染佔 38%，免疫因素佔 30%，子宮頸閉鎖不全佔 16%，子宮異常佔 14%，母親合併症（如子癇前症）佔 10%，外傷或手術佔 8%，胎兒異常佔 6%，而沒有其他致病因素的則僅佔 4%。除了可能由於本文為回溯性的研究，在方法學上，登錄資料的完整一致性可能有較大的變異。此外，種族與生活型態上的差異也是值得考慮的。

# 周產期與母體死亡率

## 周產期死亡率

以週數而論，由二十至三十六週生產之早產兒，其周產期死亡率為 10.52%，其中二十至三十二週生產的，其周產期死亡率則為 27.4%。至於單胞胎、雙胞胎、三胞胎與四胞胎在二十至三十六週生產的早產兒之周產期死亡率分別為 10.68%、7.30%、9.06%、6.82%，並沒有因胞胎的數目而影響其早產兒之周產期死亡率。

## 母體死亡率

台灣地區生產之母體死亡率已由 1952 年的每十萬個活產中的 196.56，降到 1985 年的 9.85。這次的統計中，這六家醫院在二十至三十六週間共計 10,890 產次，有 15 個早產產婦死亡的病例，約佔千分之 1.38。這個比例雖然偏高，但由於本文中的六家醫院均為二級或三級的轉送中心，兼之早產常合併有較嚴重的產科併發症，因此可能有較高的母體死

亡率。

## 早產兒死亡率與照護

由早產兒伴隨而來的新生兒急慢性問題相當多，全身各系統均有可能受到影響，其中包括肺部的新生兒呼吸窘迫症侯群、間質肺氣腫，心臟血管系統的開放動脈導管，中樞神經系統的呼吸停止、顱內出血、體溫過低，腸胃系統的壞死性腸炎、餵食問題，及對葡萄糖、膽紅素與鈣質代謝的不正常。在我們這次的統計中，有 13.53%的早產兒需被轉送到新生兒加護病房。

此外，在討論新生早產兒的照護問題時，我們也必須瞭解目前新生早產兒的存活率與罹病率。以台北馬偕紀念醫院新生兒加護病房而言，1996 年新生兒的存活率，若以妊娠週數而言，則如表 3：在 22 週前出生的新生兒均無能夠存活者，28 週有 75%的新生兒存活，31 週後則可達 95%以上。若以出生體重來看（表 4），小於 500 公克的早產亦無能夠存活者，801-900 公克的早產兒則有 71%的存活率，901-1000 公克的早產兒則有 89%的存活率，若達 1500 公克則其存活率在 90%以上，而在 1500-2500 公克的低出生體重早產兒則其存活率也有 90-100%，至於大於 2500 公克的早產兒則有 92.5%。與以前比較，這樣的新生兒存活率已有顯著的提升，在近幾年（1993-1996 年間）台北馬偕醫院低於 1000 公克的新生兒之存活率如圖 5 所示，整體而言，呈現一個上升的趨勢；馬偕醫院小兒科的林嘉相等人也曾發表對於 1987 年出生體重低於 1500 公克嬰兒之臨床研究[9]，文中出生體重在 500-799 公克者存活率為 0，800-999 公克者存活率為 46%，1000-1249 公克者為 83%，而 1250-1500 公克則為 81%。至於主要死亡原因則以顱內出血（55%）及肺玻璃膜症與其併發症（32%）最多。而台大醫院的經驗更顯示，目前早產兒的存活率已有明顯的成長，出生體重 1500 公克以上的早產兒其存活率已高達 97%，出生體重不足 1500 公克的早產兒其存活率由 1991 年的 83%增至 1996 年的 94%，而體重不足 1000 公克者其存活率由 1991 年的 43%增至 1996 年的 60-70%。

# 討　論

早產的病理生理學目前還不是很清楚；正因如此，一些治療的性質也不明白，藥物治療的效果也不是很理想，更沒有有效預防的方法。在美國近幾年來早產兒的發生率一直相當穩定。多在 5-10%，不過事實上，發生率也隨著州與州及醫院的不同而有變化。在此次的統計中，我們也可發現，不同的醫院有著不同的發生率與趨勢；同時，由於這次的六家醫院多為轉送中心，會有較多早產的轉送病例，以致早產所佔的比例可能比一般族群為多，因此，如此估算出來的發生率也可能略高。此外，隨著目前人工生殖科技的推陳出新，多胞胎妊娠的發生率在近幾年有增加的現象，而多胞胎妊娠的早產機率原本就較高，因此可能造就未來早產的發生亦會增加。

那麼我們要如何才能降低早產的發生率？可能直接引起早產陣痛的原因包括：子宮頸、陰道感染，子宮頸閉鎖不全，子宮畸形，子宮過度膨脹，母體併發症，胎兒窘迫，或由於對催產素的敏感度增加等等。一般在早產陣痛的病例中，大約只有 25%可以找到較肯定的原因。因此，想要找到有效的預防方法，似乎是相當困難；惟有針對較可能早產之高危險孕婦，予以適切的教育，以及早留意早產跡象，如此或能略收成效。至於那些產婦是處於高危險群？根據 Creasy 於 1980 年提出的預測計分法[10]，包括 37 個危險因子，而若孕婦計分為 10 分以上則為高危險群。最近 Holbrook 則將其加以簡化[11]，如此仍保留相近的效力 14.1%的孕婦會被認定是高危險群，其 Sensitivity 為 41%，陽性預測率為 24.6%。根據這項計分法，凡具有主要早產因子之一或兩項次要因子即應認定為高危險群。主要因子共 12 項，包括：多胞妊娠、曾有早產分娩者、曾有早產陣痛但足月分娩、妊娠期間腹部手術、DES 暴露者、羊水過多、子宮畸形、子宮頸錐狀切除者、子宮敏感曾因疑似早產陣痛入院者、32 週時子宮頸擴張逾 1 公分、32 週時子宮頸薄化逾 50%、及一次以上之妊娠中期流產者。次要的早產因子則共有 6 項：妊娠期間之發燒疾病、妊娠 12 週後之出血、有腎臟炎之病史者、吸煙每天逾 10 支、有一次妊娠中期流產者、多於 2 次之妊娠初期流產者。不過，如此的預測計分系統仍僅能提供部分的協助。因此，一些輔助的方法也正陸續研究中，像是藉由偵測子宮頸陰道

分泌物中之 fetal fibronectin[12]，運用超音波測量子宮頸長度 [13]，及在家宮縮監測 [14] 等，但這些方法大多仍無足夠之效力。

這次我們也嘗試尋找一些與早產相關的產科因素，例如：前置胎盤、胎盤早期剝離、產前早期破水、子癇前症、子宮頸閉鎖不全、子宮異常、胎兒異常、及絨毛羊膜炎等，在台灣還是以沒有伴隨其他產科合併症者較多。Romero 等人也曾報告指出 [15]，有三分之一的早產是源於早發性陣痛，三分之一是源於產前早期破水，另外三分之一則是因為母親或胎兒之併發症所致（表 5）。Meis 等人則指出 [16]，必須依賴較多社會經濟援助的病患，產前早期破水所佔的比例會增加，而若其經濟大多能自給自足者，則以沒有其他合併症的早產為多。若據此，似乎說明台灣目前由於經濟的高度成長，公共衛生的進步與產檢的普及，在早產的發生也偏向於單純無其他合併症者；不過關於這點，尚需更進一步的研究來釐清。

另一個值得重視的課題，在於如何增加早產兒的存活率。儘管在目前早產兒的照護方面，其存活率已有明顯的提升，但隨著醫療科技的進步，新生兒加護中心的持續發展及新技術的不斷開發，我們不難想見，低出生體重兒的存活率仍有增加的可能。此外，由台灣地區有關低出生體重兒的文獻報告中不難發現 [3,9,17,18,19]，院外轉送的病例有較高的死亡率。主要的原因還是因為台灣地區新生兒轉送系統仍不完善，若能將高危險群孕婦及早轉送至有完備新生兒加護中心的醫院待產，再加上新生兒加護中心的細心照顧，或許可以再提昇本地區低出生體重兒的存活率。

正因為現今新生兒之存活率提高，這些未足月的早產兒，因在身體大部份器官系統尚未發育完全成熟前，即已呱呱落地，當面臨外界不良的刺激與環境時，由於生理功能的不穩定，後遺症及殘障的發生率仍高。除了積極的預防外，發生早產陣痛後之產科處理，相對的也就愈發重要。目前對早產陣痛之處理為診斷一旦確立即給予藥物治療；但若於陣痛發生前使用宮縮緩解藥物，冀圖預防早產，研究結果顯示，不論就生產時之妊娠週數，或平均嬰兒出生體重均無異 [20]。若是早產合併早期破水 (PPROM)，可使用超音波，觀察剩餘羊水量之多少與子宮頸變薄、擴張及長度，能有效評估安胎是否成功及提供較佳的臨床處理 [21]；但對於 PPROM 之處理仍有許多不同的爭論，包括：是否使用抗生素？是否使用安胎藥物？是否使用類固醇？B 型鏈球菌之培養與預防？分娩方式的選

擇？這些爭論已數十年，基本上出生週數與體重仍是取決於新生兒存活之最重要因素，妥善處理 PPROM，避免感染，及分娩時妥善之新生兒急救，才能減少後遺症[22]。

如同生產一般，早產仍有相當多未知的領域值得探索。而只要人類繼續生產，早產兒就很難避免。在台灣，每年花費在早產兒照護的醫療費用仍未見減少；因早產兒而造成的產婦焦慮、生理不適、及家庭、社會問題也是值得深思的。因此，我們必須更深入去研究早產的相關課題；惟有瞭解得愈透徹，在治療方面及預防上，才能更有進展。本文雖然盡力提供關於台灣早產之相關數據，但回溯性統計仍恐以偏蓋全，將來更大規模、前瞻性的研究，以提供更完備的資料是必需的。

## 表 1. 1987-1996 年間台灣地區六大醫院之早產

| | 慈濟 | 台北榮總 | 三總 | 台北長庚 | 台北婦幼 | 台北馬偕 | Total |
|---|---|---|---|---|---|---|---|
| 統計年份 | 1987-96 | 1987-96 | 1992-96 | 1990-96* | 1987-96† | 1992-96 | |
| 總產次 | 7119 | 27106 | 7648 | 26075 | 46672 | 27683 | 142303 |
| 單胞胎生產數 | 6994 | 26852 | 7541 | 25704 | 46365 | 27395 | 140851 (98.9%) |
| 雙胞胎生產數 | 122 | 219 | 103 | 352 | 296 | 259 | 1351 (0.95%) |
| 三胞胎生產數 | 3 | 33 | 4 | 17 | 8 | 28 | 93 (0.065%) |
| 四胞胎生產數 | 0 | 2 | 0 | 2 | 3 | 1 | 8 (0.0056%) |
| 總早產數 | 549 | 2550 | 537 | 1917 | 2144 | 3193 | 10890 (7.65%) |
| 母親年齡<20 | 47 | 198 | 10 | 22 | 113 | 149 | 539 (4.95%) |
| 母親年齡≥35 | 56 | 499 | 113 | 367 | 286 | 570 | 1891 (17.36%) |
| 胎次 | | | | | | | |
| 1 | 214 | 998 | 268 | 921 | 933 | 1453 | 4787 (43.96%) |
| 2 | 192 | 861 | 208 | 734 | 833 | 1299 | 4127 (37.90%) |
| 3 | 99 | 515 | 51 | 213 | 298 | 203 | 1379 (12.66%) |
| ≥4 | 44 | 176 | 8 | 47 | 80 | 238 | 595 (5.46%) |
| C/S rate | 42.99% | 45% | 37.33% | 49.31% | 30.68% | 40.66% | 41.13% |
| 單胞胎早產數 | 474 | 2240 | 493 | 1742 | 1996 | 2923 | 9868 |
| 雙胞胎早產數 | 72 | 279 | 41 | 161 | 138 | 245 | 938 |
| 三胞胎早產數 | 3 | 29 | 3 | 12 | 7 | 24 | 78 |
| 四胞胎早產數 | 0 | 2 | 0 | 2 | 3 | 1 | 8 |

*長庚醫院 1990 年資料僅登錄 7 月 1 日至 12 月 31 日。

† 台北市立婦幼醫院 1987 年資料為 1 月至 6 月，1996 年資料亦僅包含 1 月至 6 月。

## 表 2.產科因素

| 產科因素 | 慈濟 *N* | 台北榮總 *N* | 三總 *N* | 台北長庚 *N* | 台北婦幼 *N* | 台北馬偕 *N* | Total % |
|---|---|---|---|---|---|---|---|
| PPROM | 56 | 626 | 80 | 304 | 102 | 1024 | 20.8 |
| Preeclampsia | 55 | 390 | 45 | 156 | 39 | 295 | 9.21 |
| DM | 7 | 612 | 8 | 92 | 15 | 24 | 7.25 |
| Placenta previa | 5 | 256 | 28 | 75 | 63 | 249 | 6.6 |
| Fetal anomaly | 38 | 161 | 40 | 194 | 56 | 129 | 5.86 |
| Cervical incompetence | 3 | 194 | 4 | 27 | 2 | - | 3.30 |
| Placenta abruption | 22 | 106 | 16 | 109 | 16 | 63 | 3.08 |
| Chorioamnionitis | 0 | 34 | 5 | 78 | 12 | - | 1.86 |
| Uterine anomaly | 1 | 171 | 4 | 6 | 4 | 0 | 1.77 |
| Trauma or surgery | 3 | 17 | 0 | - | 4 | 26 | 0.62 |
| Unknown | 397 | 98 | 353 | - | 495 | 1721 | 40.6 |

- 表無統計數據

表 3. 1996 年台北馬偕醫院新生兒加護病房妊娠週數別新生兒存活率

| 妊娠週數 (wk.) | 存活率 | | |
|---|---|---|---|
| | 存活數 | 總病例數 | 百分比 |
| ≤ 23 | 1 | 10 | 10% |
| 24 | 2 | 9 | 22% |
| 25 | 6 | 7 | 86% |
| 26 | 14 | 25 | 56% |
| 27 | 17 | 24 | 71% |
| 28 | 25 | 33 | 76% |
| 29 | 25 | 30 | 83% |
| 30 | 35 | 36 | 97% |
| 31 | 36 | 42 | 86% |
| 32 | 56 | 58 | 97% |
| 33 | 65 | 69 | 94% |
| 34 | 55 | 57 | 96% |
| 35 | 57 | 60 | 95% |
| 36 | 78 | 80 | 97.5% |

表 4. 1996 年台北馬偕醫院新生兒加護病房出生體重別新生兒存活率

| 出生體重 (gm) | 存活率 | | |
|---|---|---|---|
| | 存活數 | 總病例數 | 百分比 |
| ≤500 | 0 | 7 | 0 |
| 501-600 | 1 | 6 | 17% |
| 601-700 | 1 | 7 | 14% |
| 701-800 | 5 | 11 | 45% |
| 801-900 | 10 | 14 | 71% |
| 901-1000 | 16 | 18 | 89% |
| 1001-1100 | 14 | 18 | 78% |
| 1101-1200 | 18 | 23 | 78% |
| 1201-1300 | 21 | 26 | 81% |
| 1301-1400 | 24 | 28 | 86% |
| 1401-1500 | 29 | 31 | 94% |
| 1501-1600 | 27 | 30 | 90% |
| 1601-1700 | 36 | 38 | 95% |
| 1701-1800 | 29 | 31 | 94% |
| 1801-1900 | 19 | 19 | 100% |
| 1901-2000 | 25 | 27 | 93% |
| 2001-2100 | 34 | 35 | 97% |
| 2101-2200 | 31 | 31 | 100% |
| 2201-2300 | 34 | 38 | 89% |
| 2301-2400 | 22 | 23 | 96% |
| 2401-2500 | 49 | 51 | 96% |
| ≥2500 | 395 | 427 | 93% |

表 5.早產的伴隨因素

| Romero et al, 1989<br>New Haven, Connecticut | Meis et al, 1987<br>North Carolina | |
|---|---|---|
| | Public Assistance | Private care |
| 1/3 Preterm labor | 34% Preterm labor | 55% Preterm labor |
| 1/3 Preterm PROM | 46% Preterm PROM | 27% Preterm PROM |
| 1/3 Maternal or fetal complication | 20% Medical complication | 18% Medical complication |

**圖 1. 逐年發生率（1987-1996）**

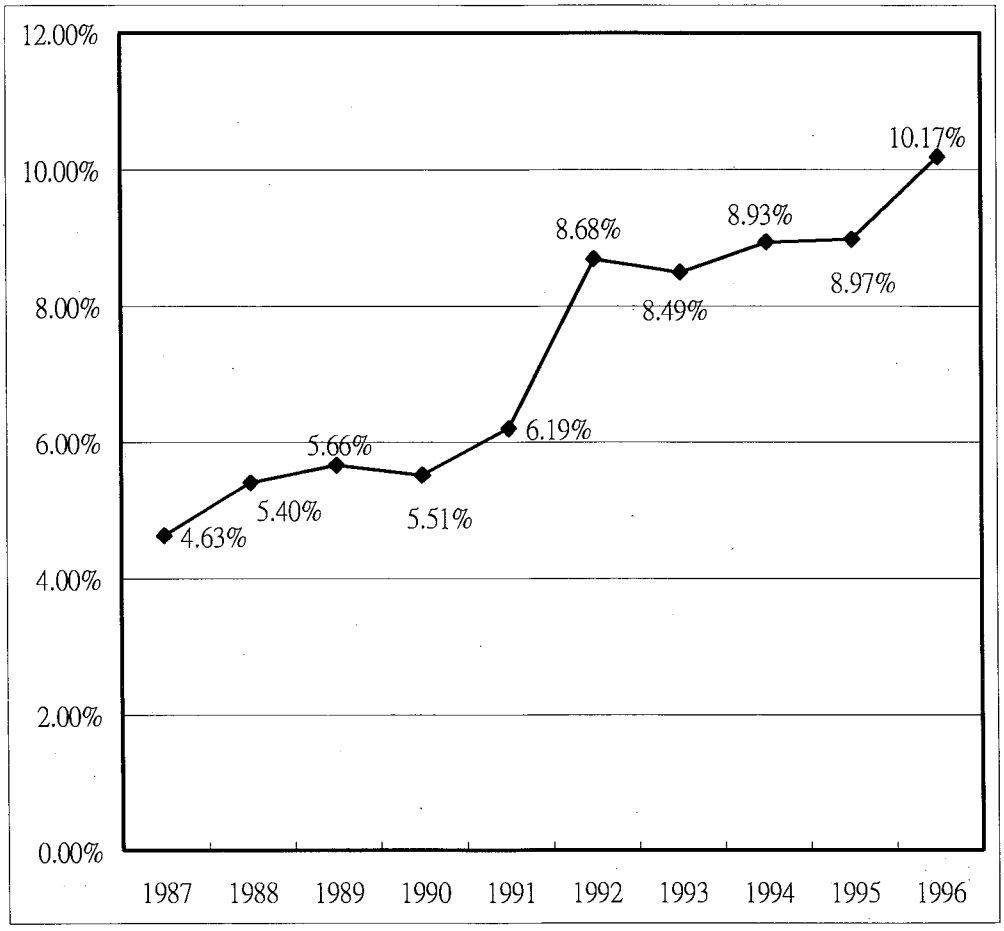


**圖 2.各醫院早產發生率（1987-1996）**

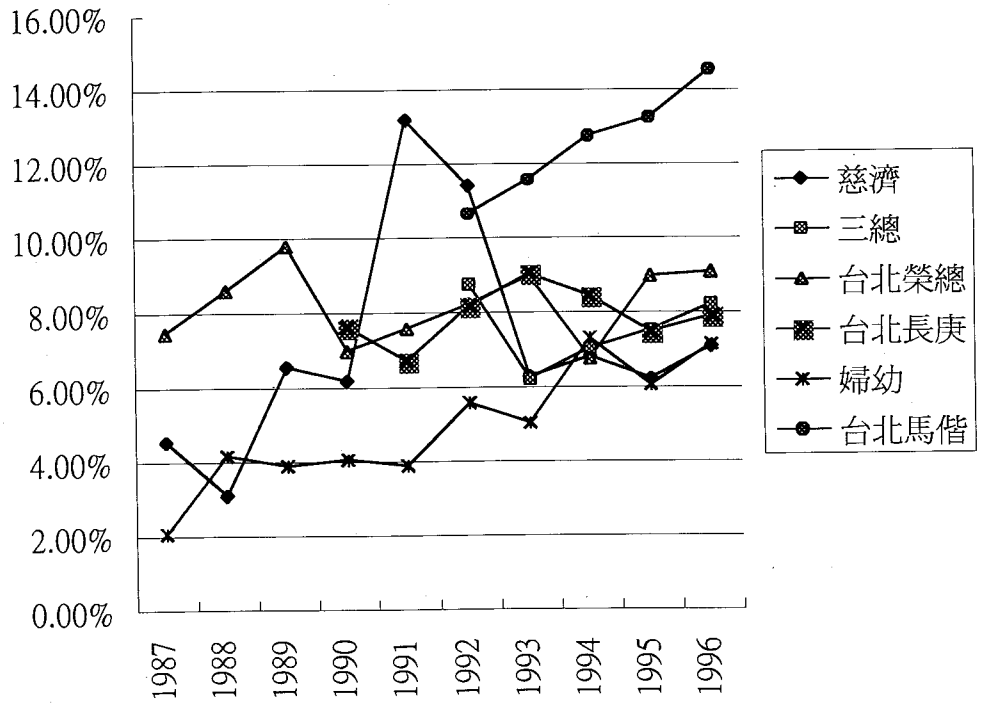



**圖 3.妊娠週數別發生率（1987-1996）**

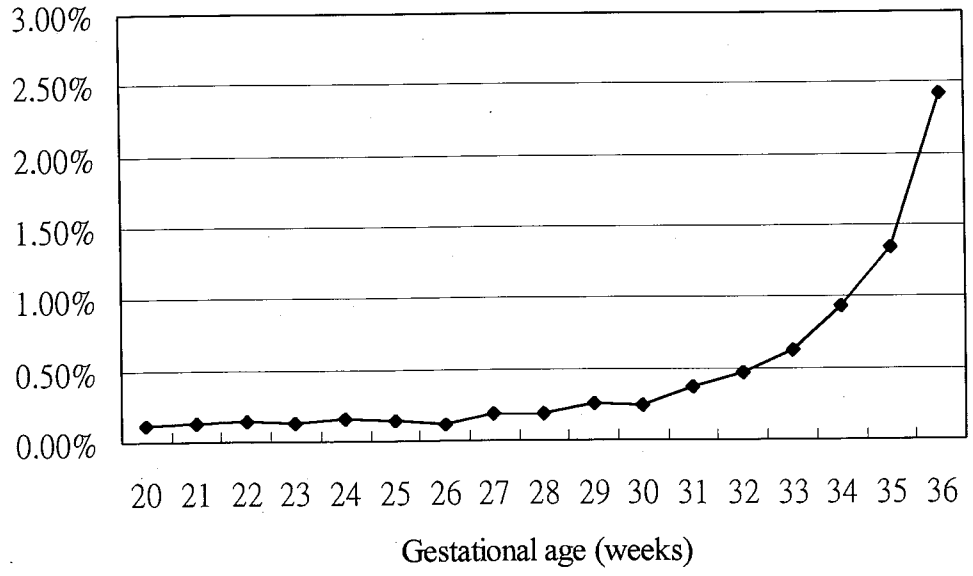


圖 4.出生體重別發生率（1987-1996）

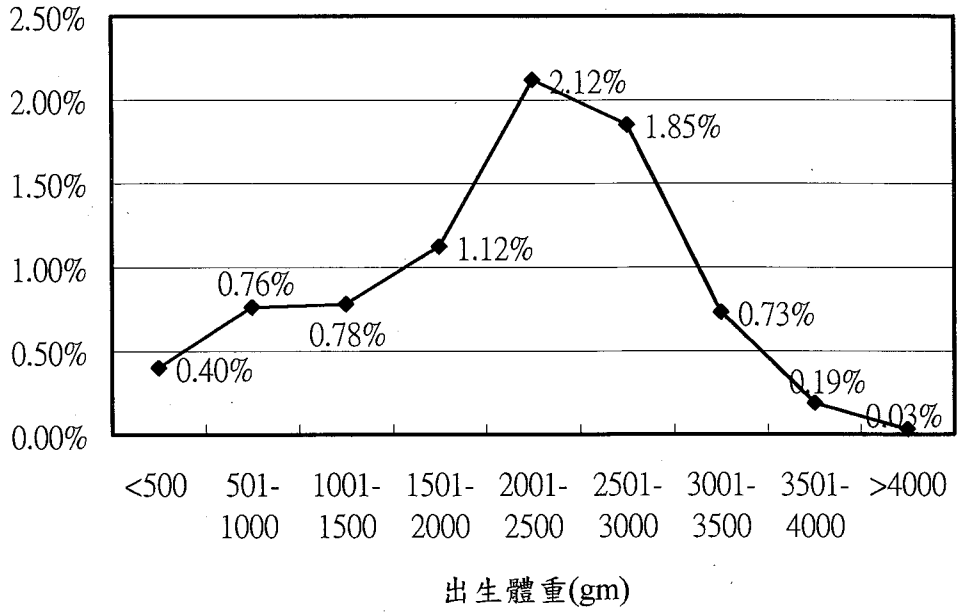
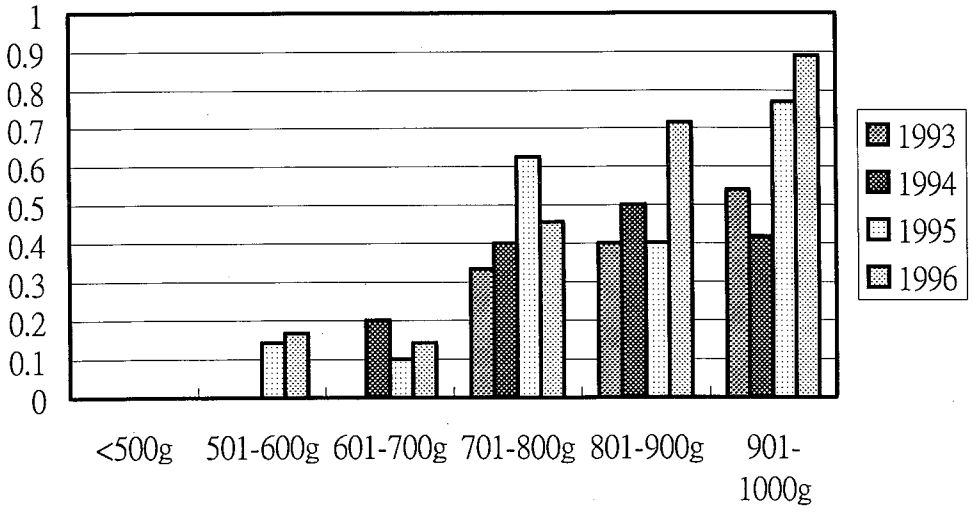



圖 5.1993-1996 年間台北馬偕醫院出生體重低於 1000 公克新生兒之存活率



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