THE EFFECT OF PRENATAL DIAGNOSIS ON THE INCIDENCE OF DOWN SYNDROME LIVEBIRTHS IN THE SINGAPORE GENERAL HOSPITAL

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ABSTRACT

During a 3-year-period between January 1988 and December 1990, there were 12 Down Syndrome (DS) livebirths out of 13, 794 livebirths at the Department of Obstetrics and Gynaecology, Singapore General Hospital, giving an incidence of 1 in 1, 150 livebirths or 0.87 per thousand.

There were 1569 mothers who were 35 years or older at the expected date of delivery (EDD) and 5 of these 12 DS livebirths were from these older mothers. Although only 11.5% of all mothers were 35 years or more, as a group, these older mothers contributed to 42% of the DS livebirths.

There were 5 DS fetuses diagnosed prenatally and 4 were aborted electively. The fifth DS fetus which was diagnosed prenatally was allowed to continue to term because of the mother's religious objection to an induced abortion.

The failure to offer prenatal diagnosis and selective procreation to all mothers 35 years or older had resulted in 4 unnecessary DS births, reducing our DS detection rate by a factor of 33%. All these 4 cases were booked late for antenatal care.

Keywords: Down Syndrome, incidence; prenatal diagnosis, preventive measures.

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INTRODUCTION

There is no question that the birth of a child with Down Syndrome (DS) would pose a social, moral and economic burden to the family and the community. Even if the outcome of a DS fetus is that of a late abortion, intrauterine death and its subsequent stillbirth or a neonatal death, the accompanied medical complications are distressing to the parents and the doctors. The frustration and disappointment of the attending doctors and nurses, especially if delivery is by Caesarean Section, are considerable and it is in the interest of the perinatal team concerned to prevent the birth of a DS baby.

OBJECTIVES

The main objective of this paper is to examine the effect of prenatal diagnosis on the prevention of DS livebirths in the Singapore General Hospital over a period of 3 years from January 1988 to December 1990. Improvement to the current practice of antenatal care in relation to prenatal diagnosis of DS is also discussed.

METHODOLOGY

The obstetric data of all deliveries in the 3-year-period 1988 to 1990 in the Department of Obstetrics and Gynaecology were analyzed. Maternal, fetal and peripartum information were captured on personal computers installed with programmes designed and written by us (YSH et al). The OUR (Obstetric Ultrasound Registry) captured the relevant fetal data during each ultrasound scan done. The FMP (Fetal Medicine Procedure) captured the data during invasive prenatal diagnostic procedures. The PPDB (Peri-Partum Data Base) captured the peripartum events and outcome.

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All babies were routinely screened by the paediatricians of the Neonatology Department. Diagnosis of DS was made on clinical grounds and confirmed by karyotyping. All DS babies were registered in our DS Registry in the Fetal Medicine Database.

Chorionic Villus Sampling (CVS), amniocentesis, Fetal Blood Sampling (FBS) were available at our hospital since January 1987. Mothers who were at a higher risk of delivering a baby with a chromosomal abnormality and booked before the 20th week of gestation were routinely counselled for these procedures. The concept of selective procreation was discussed. The quoted risks of DS at birth and at amniocentesis were those shown in Table I. Selection for the most suitable prenatal diagnostic procedure was based on the patient's choice after elaborate counselling on the balance of risks between procedure associated fetal loss, the timing of the procedure as well as individual characteristics like age, parity and fertility of the mother. Mothers who booked after the first trimester ie after 12 weeks would be counselled for amniocentesis only. The karyotype was disclosed to the parents when a DS was diagnosed. The option of induced abortion was completely left

Table I
Age Specific Incidence Of DS
At Birth And At Amniocentesis

Maternal Age	At Birth	At Amniocentesis
20	1:1, 500	1:1, 200 (E)
25	1:1, 350	1:1, 000 (E)
30	1:900	1:700 (E)
35	1:380	1:256
37	1:240	1:156
39	1:150	1:96
41	1:85	1:59
43	1:50	1:36
45	1:28	1:22

(E) = estimates
Compiled and modified from figures quoted by Connor [7], Ferguson-Smith [2] and Hook [8].

to the parents. Karyotyping was also offered to pregnancies with structural abnormalities even when the gestation is above 20 weeks. The age distribution of all patients delivered in our department were analyzed. The total number of livebirths during the January 1988 and December 1990 was used as the denominator.

RESULTS

There were a total number of 317 amniocentesis, 113 CVS and 13 FBS done for the purpose of karyotyping during the period of study. Of these, 267 amniocentesis, 91 CVS and 3 FBS were done purely for the indication of advanced maternal care. The other indications were tabulated in Table II.

Table II - Indications For Karyotyping January 1988 To December 1990

Indications	Amniocentesis	CVS	FBS	Total
Maternal age 35 & above (age only)	267	91	3	361
Past or family history suggestive of DS	21	11	0	32
Age and past/family history (combined)	24	1	0	25
Fetal anomaly	2	1	7	10
Others	3	9	3	15
Total	**317**	**113**	**13**	**443**

Mothers with previous infertility tend to favour amniocentesis which has a lower procedure associated fetal loss and many multiparous women who booked early opted for CVS. Amniocentesis was the more popular method partly due to the late antenatal booking pattern. More than 80% of all mothers counselled by us accepted prenatal diagnosis of DS. Most of the decliners did so because of religious objection to induced abortion.

Overall incidence of DS livebirths

During the period January 1988 to December 1990 there were 12 DS livebirths out of 13,794 livebirths. This gave an overall incidence of 0.87 per thousand livebirths or 1 in 1,150 livebirths. The incidence of DS livebirths is generally accepted to be about 1 in 800 livebirths[1,2]. Table III compares the incidence in different countries[3-6].

Table III - Incidence of DS Livebirths

		Number per thousand livebirths	
In Singapore General Hospital		0.87	(1:1, 150)
January 1988 - December 1990			
No of DS livebirths	12		
Total No of livebirths	13,794		
In Hong Kong		0.898	(1:1, 114)
In Malaysia		1.04	(1: 959)
In Australia		1.45	(1: 690)
In England/Wales		0.73	(1:1, 370)

DS diagnosed in-utero

There were 5 DS fetuses diagnosed antenatally. Two were diagnosed by CVS and three by amniocentesis. The outcome of these pregnancies are shown in Table IV.

Table IV - Maternal and Gestational Age at Antenatal Booking All DS Cases - Livebirths and Aborted Fetuses January 1988 to December 1990

No.	Maternal Age	Gestation at Booking	Remarks
1	20	31.5	Maternal age
2	24	30.0	less than 35
3	24	30.3	
4	24	34.2	
5	28	37.0	
6	29	26.0	
7	30	36.0	
8	35	38.0	Age 35 or more
9	37	34.4	and booked
10	39	36.0	late
11	42	31.3	
12	40	9.4	Age 35 or more
13	41	11.6	CVS done
14	41	7.2	Age 35 or more
15	43	8.5	Amniocentesis
16	39	17.0	done

NB Cases No 12-15 had termination of pregnancy done. Case No 16 was a case of DS diagnosed prenatally and later delivered at term. The mother changed her decision to abort the DS baby.

Maternal Age and the Incidence of DS livebirths

In this study, 7/12 or 58% of DS livebirths were born from mothers younger than 35 years old and 5/12 or 42% were from mothers aged 35 years or older. The maternal age distribution during this period showed that 11.5% of women delivered in the Singapore General Hospital were 35 years or older (Table V).

Table V - Maternal Age Distribution Pattern At The Singapore General Hospital January 1988 to December 1990

Age Interval	No. DS Births	(%)	No. Total Births	(%)
less than 20	0	(0)	207	(1.5)
20 to 24	4	(33.3)	2,717	(19.7)
25 to 29	2	(16.7)	5,590	(40.5)
30 to 34	1	(8.3)	3,711	(26.8)
Subtotal	7	(58.3)	12,225	(88.5)
35 to 39	4	(33.3)	1,324	(9.6)
40 to 44	1	(8.3)	234	(1.8)
more than 44	0	(0)	11	(0.1)
Subtotal	5	(41.7)	1,569	(11.5)
Total	**12**	**(100)**	**13,794**	**(100)**

Gestation at Booking and the Incidence of DS livebirths

Table IV showed that a majority of patients who had DS livebirths had late obstetric booking or were not booked at all (unbooked). Some of these mothers were seen by primary health doctors much earlier but not referred for prenatal diagnosis.

DISCUSSION AND CONCLUSION

The incidence of DS livebirths in our study compares well with incidences in Hong Kong[3], Australia[4], England & Wales[5], and Malaysia[6] (Table III). The generally accepted overall incidence at birth is 1 per 800 livebirths. The incidence is well established to be age specific and increases with maternal age [7,8]. In Singapore, women still booked late or do not book at all for antenatal care. All but one of the DS livebirth in our study did not book early enough to have prenatal diagnosis.

If all pregnancies at risk were to book by the 8th week of amenorrhoea, it would be possible to offer prenatal diagnosis either by CVS or amniocentesis. However, even if booking is made only at the second trimester, amniocentesis and selective procreation are still feasible up to 19 to 20 weeks. FBS (cordocentesis) may be offered for rapid karyotyping[9] of selective pregnancies up to 22 weeks considering that the legal limit of abortion is up to 24 weeks gestation[10].

With all these methods available, our older mothers should have a higher utilisation of prenatal diagnosis. Some of the reasons for this default may include lack of awareness, fear, religious or ethical objections to abortions[11]. Perhaps we, as professionals, have failed in our duty to disseminate accurate information and arouse public awareness about prenatal diagnosis.

Better trained staff and a lower procedure-associated complication rate may alleviate fears of the loss of a normal fetus. Early booking should be strongly encouraged and shared antenatal care programmes involving the primary health care doctors would give an even better rate of detection of DS.

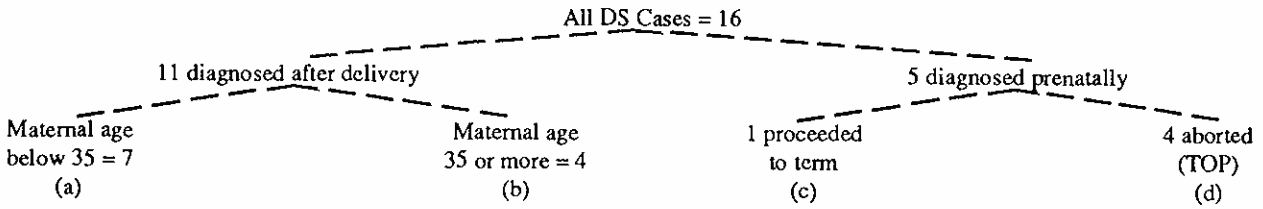
Non invasive screening tests by means of ultrasonography[12] combined with maternal serum alpha feto-proteins[13], unconjugated estriol[14,15] and beta hCG[16] may be used to select younger patients for amniocentesis. We have examined these and are concordant with most world authorities that the lack of prospective studies on the benefits of these screening tests made them premature for clinical application. The papers published to date were largely a result of retrospective epidemiological analysis of tests never designed for the purpose of DS screening[12-16]. Nevertheless, these tests deserved to be seriously considered for research[17].

In the last 3 years, our DS incidence was not affected by our status as a tertiary referral centre. None of the DS livebirths delivered was from these referred patients. However, if all the 5 cases of DS fetuses diagnosed in utero were to end as livebirths, the incidence would have been much higher.

In this three-year-study, mothers 35 years or older at EDD contributed to 42% of DS livebirths. This figure is higher than the usual estimated 20 to 30% quoted elsewhere[18-20]. If all mothers at 35 years or older were to have prenatal karyotype performed, up to 42% of DS livebirths in this 3-year-study could be detected. If these DS fetuses were aborted, the corrected DS incidence would then be 1 in 1970 livebirths. On the other hand, if all the 4 electively aborted DS fetuses were to be born alive, the DS incidence would be 1 in 862 livebirths. Even if we assume a 15% to 20% natural attrition rate to all DS pregnancies after prenatal diagnosis and only 3 out of these 4 electively aborted DS fetuses were to have been born alive, the incidence would then be 1 in 920 livebirths (Fig 1). This is double the occurrence of DS livebirths if all mothers aged 35 or above were to have prenatal diagnosis offered. The need for prenatal diagnosis must be reiterated for mothers above 35 years of age on the expected date of delivery.

DS is an imminently preventable birth defect. There is still a lot to be done to prevent undue social and economic burden

Fig 1
Effect of Prenatal Diagnosis on the Incidence of DS Livebirths in the Singapore General Hospital January 1988 to December 1990



Hypothetical Situation A: If all mothers 35 years or older were to have prenatal karyotype performed, up to 42% of DS livebirths in this study could be detected. If these DS fetuses were aborted, the corrected DS incidence would then be 1 in 1,970 livebirths.

$$\text{Incidence A} = \frac{a}{13794 - b - c} = \frac{1}{1970}$$

Hypothetical Situation B: If all the 4 electively aborted DS fetuses were to be born alive, the DS incidence would be 1 in 862 livebirths.

$$\text{Incidence B} = \frac{a + b + c + d}{13794 + d} = \frac{1}{862}$$

Hypothetical Situation C: Even if we assume a 15% to 20% natural attrition rate to all DS pregnancies after prenatal diagnosis and only 3 out of the 4 electively aborted DS fetuses were to have been born alive, the incidence would be 1 in 920 livebirths.

$$\text{Incidence C} = \frac{a + b + c + (d-1)}{13794 + (d-1)} = \frac{1}{920}$$

Actual Incidence: The actual incidence of DS livebirths in this 3 year period was 1 in 1,150.

$$\text{Actual Incidence} = \frac{a + b + c}{13794} = \frac{1}{1150}$$

to parents as well as the community and to have better distribution of our limited medical resources. Preventive measures to reduce the incidence of DS livebirths must be instituted by a coordinated effort between the doctors in primary health care and the doctors in the fetal medicine sub-speciality.

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