

# Anencephaly in Singapore: a ten-year series 1993–2002

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## ABSTRACT

**Introduction:** Anencephaly is a neural tube defect that is incompatible with life. Previous studies have suggested that there is a racial predilection for this condition. However, local studies have not shown a statistical difference between the races. The aim of this study is to examine the incidence and the demographical trend of this condition over a ten-year period.

**Methods:** Data of patients with anencephaly born from 1993 to 2002 were retrieved from the National Birth Defect Registry and analysed.

**Results:** There were a total of 267 cases of anencephaly in the ten-year period from 1993 to 2002, giving an overall incidence of 0.58 per 1,000 livebirths, with a decreasing trend noted. The incidence was highest among the Malay population, compared with the Chinese population (p-value equals 0.03) and other races. Abortion rates have also increased over the years, causing a reduction in livebirth rates for this condition.

**Conclusion:** The overall incidence and birth incidence of anencephaly has seen a decreasing trend over the last ten years, with the latter being contributed significantly by early termination. More studies should be done to ascertain if improved folate supplementation has contributed to the drop in overall incidence. The incidence in the Malay population is significantly higher than other races and this phenomenon should be further examined.

**Keywords:** anencephaly, birth defects, neural tube defects, termination of pregnancy

*Singapore Med J 2007; 48(1):12–15*

## INTRODUCTION

Neural tube defects (NTD) account for 4% of all notified

congenital birth defects in Singapore, with an incidence of 0.91 per 1,000 livebirths in the period 1993–2002. Of these neural tube defects, the two major conditions are spina bifida and anencephaly, with the latter accounting for 63% of cases with NTD<sup>(1)</sup>. While 80–90% of infants with spina bifida survive into adulthood with varying degrees of morbidity, anencephalic foetuses are incompatible with life, with the majority perishing within the first 24 hours of life. A previous study<sup>(2)</sup> has suggested that there might be a racial difference in the incidence of NTD, with a higher predilection noted among the non-white populations. Ho in 1991 showed that among the Asian population in Singapore, the Malays appeared to have a higher incidence of anencephaly, although this finding was not statistically significant<sup>(3)</sup>.

Since the 1990s, folic acid supplementation (400 microgrammes) has been shown to be beneficial in reducing the incidence of NTD by 50–70%, and much work has been done to educate as well as implement folate fortification of food in the United States and other parts of the world<sup>(4)</sup>. Locally, folic acid supplementation has been increasingly given to expecting mothers in the first trimester of pregnancy. The aim of this paper is to look at the incidence and the demographical trend of this condition over a ten-year period.

## METHODS

The method of data collection at the National Birth Defect Registry (NBDR) has been previously described<sup>(5)</sup>. Multiple sources comprising government bodies, public and private medical centres contribute to the collection of birth defect data. These include the Epidemiology and Disease Control (E&DC) Division of the Ministry of Health, the National Registry of Births and Deaths (RBD), as well as cytogenetic and histology laboratories, and nursery wards in both public and private hospitals in Singapore. Using an in-house database software programme, NBDR Version 1.0, developed with the Information Service Department of the KK Women's and Children's Hospital, all notified cases of anencephaly from 1993 to 2002 were extracted from the registry's database, and the original notification forms were retrieved from the registry. Data from these forms were then analysed. Care was taken to ensure confidentiality and anonymisation of extracted and analysed data. The population denominators

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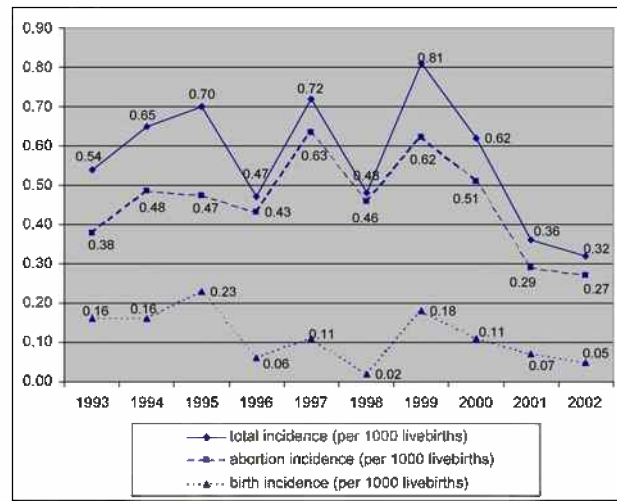
used in computing the rates per 1,000 livebirths shown in the tables were obtained from the Reports on Registration of Births and Deaths<sup>(6)</sup>.

## RESULTS

Between 1993 and 2002, a total of 267 cases of anencephaly were notified. In the same period, there were 460,532 livebirths<sup>(6)</sup>, giving an overall incidence of 0.58 per 1,000 livebirths. An analysis of the trend over the ten-year period suggests a decrease in total incidence from 0.54 per 1,000 livebirths in 1993 to 0.32 per 1,000 livebirths in 2002, with a consistent decrease from 1999 onwards (Fig. 1). The race-specific incidence of anencephaly was 0.76 per 1,000 livebirths in the Malay population, higher compared to 0.55 per 1,000 livebirths in the Chinese population ( $p=0.03$ ), and 0.50 per 1,000 livebirths in the Indian population ( $p=0.1$ ) (Table I).

The abortion rates for this condition differed between the races, with the lowest rates for the Malay population and the highest rates for the Chinese. This in turn resulted in higher livebirth rates for anencephaly among the Malay population (Table I). The overall trend of abortions for anencephalic fetuses over ten years from 1993 to 2002 has seen an increase from 70.4% in 1993 to 84.6% in 2002 (Table II). The incidence of anencephalic livebirths has seen a decreasing trend over the last ten years, from 0.16 per 1,000 livebirths in 1993 to 0.05 per 1,000 livebirths in 2002 (Fig. 1).

Five out of 267 women (1.9%) had a previous baby with congenital malformations, of which three had anencephaly, one had hydrocephalus and one had multiple malformations. Maternal medical illnesses include asthma (6/267), epilepsy (2/267), gestational diabetes mellitus (3/267), thyrotoxicosis (2/267), thalassaemia minor (2/267) and adrenal failure (1/267). One woman had a history of chicken pox at eight weeks of gestation. The medical history was unknown in ten cases. The mean maternal ages were 28–30 years, across all races (Table III).



**Fig. 1** Total, abortion and birth incidence rates (per 1,000 livebirths) for anencephaly cases from 1993 to 2002.

Out of 267 cases of anencephaly, 25 cases (9.4%) were associated with other congenital malformations. Of these 25 cases, 12 had single malformations and 13 had multiple malformations. Fig. 2 shows the different types of associated malformations by systems.

Interestingly, five out of 25 (20%) had omphalocele/exomphalos. There were 34 livebirths, of which 20 (58.8%) were male and 14 (41.2%) were female. Their mean gestation was 37.2 +/- 4.3 (range 29–43) weeks, and their mean birth weight was 2,090 +/- 834 (range 830–4,550) g. 23 newborns (53.5%) perished within 24 hours of birth. The longest survival was 16 days.

## DISCUSSION

The overall incidence of anencephaly during our period of study does not seem to have changed significantly from a previous local report by Tan et al in 1984, when he reported an incidence of 0.54 per 1,000 livebirths in

**Table I. Maternal ethnicity and incidence of anencephaly from 1993 to 2002.**

Ethnicity of mother	Population livebirths	Overall anencephaly cases		Abortions			Births (livebirths and stillbirths)		
		No.	Rate*	No.	%	Rate*	No.	%	Rate*
Chinese	310,656	170	0.55	157	92.4	0.51	13	7.6	0.04
Malay	85,779	65	0.76	29	44.6	0.34	26	55.4	0.42
Indian	38,187	19	0.50	17	89.5	0.46	2	10.5	0.04
Others	25,910	13	0.50	8	61.5	0.31	5	38.5	0.19
Total	46,0532	267	0.58	211	79.0	0.46	56	21.0	0.12

\*per 1,000 livebirths.

**Table II. Percentage of abortions for anencephaly cases from 1993 to 2002.**

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1993–2002
N	27	32	34	23	34	21	35	29	15	13	263
A	19	24	23	20	29	20	27	24	12	11	209
%	70.4	75.0	67.7	87.0	85.3	95.2	77.1	82.8	80.0	84.6	79.5

N: total number of anencephaly cases; A: number of aborted cases for anencephaly; %: percentage aborted

**Table III. Maternal age group and anencephaly from 1993 to 2002.**

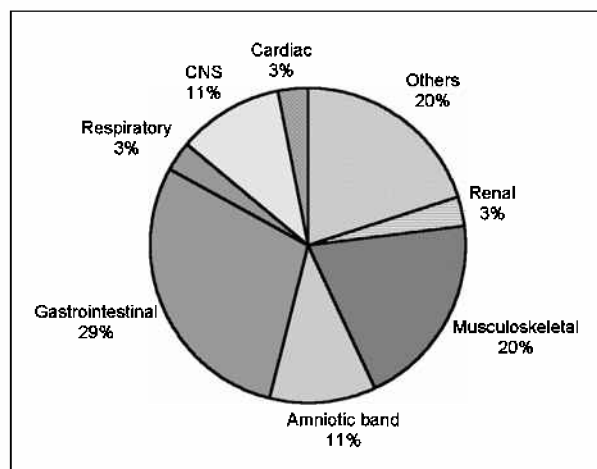
Ethnicity of mother	Population livebirths		Overall anencephaly cases		Mean age (years) ( $\pm$ SD)	Age range (years)
	No.	%	No.	%		
Chinese	310,656	67.5	170	63.7	30 ( $\pm$ 5.6)	17–48
Malay	85,779	18.6	65	24.3	28 ( $\pm$ 5.2)	18–38
Indian	38,187	8.3	19	7.1	28 ( $\pm$ 5.5)	18–35
Others	25,910	5.6	13	4.9	30 ( $\pm$ 3.2)	24–35
Total	460,532	100	267	100	29 ( $\pm$ 5.0)	17–48

the period 1976–1980<sup>(7)</sup>. An earlier report by Toh and Ho in 1977 had also shown a similar overall incidence of 0.6 per 1,000 livebirths in the period 1970–1976<sup>(8)</sup>. The decreasing incidence of total births of anencephaly from 0.54 per 1,000 livebirths in 1993 to 0.32 per 1,000 livebirths in 2002 could be attributed to an increasing usage of folic acid supplementation in the first trimester of pregnancy. Results from the Medical Research Council Vitamin Study in 1991 had established the role of folic acid in the prevention of NTD, including anencephaly<sup>(9)</sup>. In view of the protective role of folic acid, the Royal College of Obstetricians and Gynaecologists had also advocated, via its Scientific Advisory Committee in 1997, for mandatory food fortification in the UK. The consistent drop in incidence from 1999 through to 2002 in our series could be an indication of the efficacy of primary prevention through increased use of folate supplementation in the periconceptual and first trimester periods, as a

result of raised awareness among obstetricians. Prior to this period, the overall incidence of anencephaly in the local population had remained somewhat constant at 0.5–0.6 per 1,000 livebirths from 1970 to 1980. However, this association should be correlated with the incidence rates of spina bifida as well, to see if there is indeed a corresponding decrease.

The reduction in livebirth incidence of anencephaly is attributed to the increasing proportion of pregnancy terminations for this condition. As ultrasound services improve with earlier and more accurate diagnoses, and as the stigma of pregnancy terminations decrease, we have also seen an increase in termination rates, with a corresponding drop in the incidence of livebirths for anencephalic babies. This is consistent with a report by Chan et al which showed that although the total prevalence of NTD in South Australia remained stable from 1966 to 1991, prenatal diagnosis and termination of pregnancy resulted in an 84% fall in birth prevalence<sup>(10)</sup>. Secondary prevention through terminations has dramatically reduced our livebirth incidence rates over the last ten years.

There is a higher prevalence of anencephaly among the Malay population in Singapore (0.76 per 1,000 livebirths), compared with the other major racial groups. This finding is similar to a previous paper by Ho in 1991<sup>(3)</sup>. However, our study is the first to show a statistically significant difference in the incidence between the Malay and the Chinese populations. Although there is also an absolute difference in incidence rates between the Malay and the Indian populations, this was not statistically significant, possibly due to the significantly smaller numbers involved. It is interesting to note that a sub-analysis of the Chinese population with NTD by Toh and Ho in 1977 had shown a higher occurrence among Teochew babies<sup>(8)</sup>. This difference in incidence rates between and

**Fig. 2** Associated malformations

within the races could possibly suggest dietary factors and genetic predisposition for this condition, and warrants further studies.

A further analysis of this phenomenon after stratification by race showed however that the Malay population in Singapore is also less likely to terminate pregnancies complicated by anencephaly. This is likely due to religious and social reasons in which termination is not a widely-accepted option. Another possible reason could be the late or infrequent antenatal care among the Malay population<sup>(11)</sup>. Late booking at the antenatal clinic may contribute to a lower rate of induced abortion for birth defects. Another result of infrequent antenatal care would be a decreased availability to and therefore decreased intake of physician-prescribed folate. Both of these factors would likely have resulted in a higher total as well as livebirth rate of anencephaly among the Malay population. More studies should be done to ascertain the level of awareness among Malay mothers for this condition so that appropriately tailored educational programs can be planned and implemented.

In conclusion, the overall and birth incidence of anencephaly in Singapore has seen a decreasing trend in the ten-year period from 1993 to 2002. The former is likely to have been attributed to the increased awareness among obstetricians of folate supplementation as well as a concomitant increased prescription of folate in the periconceptual and first trimester periods. The latter is a result of increased termination of pregnancy for this condition. The differences in race-specific overall incidence (notably the significantly higher incidence

among Malays) warrant further studies.

## ACKNOWLEDGEMENT

The authors are grateful for the support of Dr Chew Suok Kai, Director of Epidemiology and Disease Control Division, Ministry of Health, Singapore, in this study.

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