



The Northwestern University Triplet Study I: Overview of the International Literature

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Abstract. The international literature on triplet births is surveyed. No definitive work on triplet gestations exists. The relatively few articles on this subject are divided into three categories: 1) national data; 2) local, regional or hospital series; 3) case reports. Clinical concerns, such as prematurity, low birth weight, bed rest, and tocolysis, are discussed with specific reference to literature citations.

Key words: Triplets, Prematurity, Birth weight, Bed rest

INTRODUCTION

Accurate information on the numbers of triplet deliveries is not readily available. The second survey of secular trends in twinning rates by James [25] in 1982 does not mention triplets, and the extensive bibliography which accompanies this report is devoid of direct references to the frequency of triplet births. One major American review [27] published in 1982 noted a decline in triplet births between the years 1922 and 1958. A similar trend was described in Japan between 1955 and 1967 and once again in 1974 [21]. In contrast, the rate of triplet births in Australia increased by 40% in the years 1920-1969 [8]. At present, attempts to develop a consensus about the frequency of triplets are hampered by differences in reporting methods and statistical presentations as well as the occasional need to supplant existing clinical and demographic data with theoretical calculations.

Triplets derived solely from a process of zygotic division always are of the same sex,

whereas mixed-sex triplets occur as a result of multiple ovulation [1]. In 1960 Allen [1] mathematically approached the problem of determination of the frequency of specific combinations of triplet and quadruplet zygosity. However, at that time, the concept of "vanishing twin" did not exist. In 1982, Landy et al [29] reviewed the literature on this phenomenon and subsequently Landy et al [30] confirmed observations collected from the literature by a prospective study. More recently, the term "vanishing sac syndrome" was used to describe this process in higher order multiple gestations [17]. Gindorff et al [17] reported sac to embryo reductions as follows: $2 \rightarrow 1$; $3 \rightarrow 2$; $4 \rightarrow 2$; $5 \rightarrow 3$. As a result of these findings, it is reasonable to suggest that Allen's [1] commentary may require modification to consider reductive as well as additive processes.

Human triplet gestations share many characteristics of twin births. In contrast to twin gestations which derive either from the release and subsequent fertilization of two ova or from the later division of one zygote, triplet gestations may derive from one, two or three ova [1]. Except in unusual clinical circumstances [21,34], the relative theoretical

Table 1 - Data from studies which may be representative of national data by date of publication

Ref.	Country	Year pub.	Study years	Rate/100,000		
27	USA	1962	1922-58	<u>1933-78</u> 10.21 white 9.0	<u>1952-58</u> 8.63 black 14.0	
8	Australia	1978	1920-69	<u>1922</u> 8.2	<u>1969</u> 11.5	
21	Japan	1980	1955-67; 1974	<u>1955</u> 6.6	<u>1960</u> 4.9	<u>1974</u> 5.6
23	Japan	1984	1955-67; 1974			
22	Japan	1980	1951-68; 1974			
2	Japan	1980	1975			
3	Japan	1980	1975			
4	Japan	1980	1975			
34	Nigeria	1971	1963-9			160
6	Sweden	1983	1973-81			11
13	Nambia	1984	1967-76			12.7 white; 44.3 black; 1:13.1 colored; 42.1 all

*Estimated by Allen's method (1960)

frequencies of zygosity types among triplets as well as higher orders of multiple births must be calculated. In the absence of a definitive monograph on triplet gestations, we reviewed the relatively small numbers of clinical reports. These fall into three main categories: 1) national data; 2) local, regional or hospital series; and 3) case reports. It is possible that some sources were inadvertently overlooked or were not available to us. Our primary source of references was a computer-generated list from Medlars and Medline obtained from the Archibald Church Medical Library at Northwestern University Medical School. Once obtained, these articles served as a source for obtaining secondary references.

LITERATURE REVIEW

To date there is little sustained clinical interest in presenting a continuum of national data on triplet birth rates (Table 1). Four items from the published literature are noteworthy,

Rate by type *			Sex composition tabulated	Stillbirth rates given	Comments
MZ	DZ	TZ			
1933-37			No	No	Extensive twin data presented
19.4	55.2	27.5			
1952			Yes	No	
19.9	46.8	19.6			
23.9	52.4	23.7	Yes	No	
All years			Yes	Yes	
3.2	1.8	0.4			
1974			No	Yes	Authors question effect of fertility drugs in changing rate of TZ triplets.
2.9	1.4	1.2			
				Yes	Detailed analysis of factor contributing to SB rate.
			Yes		Extensive analysis of weight and birth order. Discussion of length of triplet gestation.
			Yes		Discussion of birth weight and subsequent infant growth.
9.1	36.4	54.5			The high rate of DZ and TZ sets is unparalleled in the world and underlies interest in racial differences in levels of circulating FSH.
			Yes	No	Authors call for social and financial assistance to families.
				Yes	

Table 2 - Regional, local, and hospital series by date of publication

Ref.	Country	Year pub.	Yrs. study	No. cases	Maternal demographic data	Comb. wts.	Surv. data	Del. data	Gestational	Comment	Ultrasonic dx.
12	UK	1978	1958-1977	14	Yes	Yes	Yes	Yes	Yes		No
41	USA (Iowa)	1985	1946-1983	20	Yes	Yes	Yes	Yes	Yes	Reviews literature	No
14	Nigeria	1980	1972-1979	27	Yes	Yes	Yes	Yes	No		No
24	Australia	1979	1946-1976	59	Partial	No	Yes	Yes	Yes		No
35	USA (New Jersey)		1980-1981	4	Yes	Yes	Yes	Yes	Yes		No
33	USA (Mass.)	1981	1954-1976	15	No	Yes	Yes	Yes	Yes		No
6	Sweden*	1983	1973-1981	8	No	No	Yes	Yes	Yes		Yes
36	South Africa	1979	1967-1976	61	Yes	Yes	Yes	Yes	Yes	Merits of careful vaginal delivery are presented	Yes
38	Israel	1980	1970-1978 (6 quads)	19	No	Yes	Yes	Yes	Yes	Use of PO Ritodrine from beginning of 2nd trimester; IV only when premature contractions occur	Yes
31	USA	1982	1965-1981 (6 quads 1 quint)	27	Yes	Yes	Yes	Yes	Yes	Bed rest by 28-30 wks. Butamethasone at 26-28 wks + phenobarb routinely.	Yes
20	Israel	1982	1960-1960-31	31	Yes	Yes	Yes	Yes	Yes	Neonatal outcome of multiple pregnancy related primarily to maturity of infants.	No

(Continued)

Table 2 - *Contd.*

Ref.	Country	Year pub.	Yrs. study	No. cases	Maternal demographic data	Comb. wts.	Surv. data	Del. data	Gestational	Comment	Ultrasonic dx.
7	USA	1978	NA	10	NA	Yes	Yes	Yes	Yes	1) Safer to treat false premature labor unnecessarily than to overlook an asymptomatic progress of labor; 2) Less expensive to keep a mother hospitalized for several weeks than to treat several pre-matures in an intensive care nursery for a long time.	Yes
11	USA	1980						Na	Na	1) Should be followed by a tertiary care center; 2) Aggressive management with use of tocolysis to delay premature labor and steroids for lung maturation.	No
37	France	Not yet pub.	1975-1986	21		Yes		Yes	Yes	Elective CS seems to improve Apgar scores.	Yes
42	Belgium	Not yet pub.	1975-1986	16	Yes	Yes	Yes	Yes	Yes	Not clear as to whether or not CS has a better result than vaginal delivery.	No
Total cases										322	

* Study also listed in Table 1.
NA = not available.

however. First, triplet rates (per 100,000 deliveries) vary widely between countries. In general, they parallel the well-known differences observed for twins in which the highest rates are found in Nigeria, the middle range occurs in Caucasian populations, and the lower range occurs among Oriental races. Second, triplet zygosity varies by maternal race. In the Australian data, the frequency of MZ and DZ triplets is equal; in contrast, DZ triplets in Nigeria are more than five times as frequent as MZ triplets. Third, Japanese interest in triplets is unique; no other nation has comparable published data in the clinical literature. Lastly, a report from Sweden [6] is the only national survey that proposes giving social assistance to family units as a means of countering the potential for family dissolution from financial and emotional pressures.

Table 2 lists 15 clinical papers on triplet deliveries published since 1978. A total of 332 triplet sets are reported from deliveries conducted between 1964 and 1983. Although data are not presented in a uniform manner, reports discuss similar clinical concerns. The use of ultrasound is featured in less than 5% of these series. Comments are provided in the table for some of the studies.

Table 3 lists 14 triplet case reports published between 1974 and 1985. A variety of problems are addressed, but no specific medical concern is prominent. It is possible that other reports also exist, but as there is no registry of such reports, we are unable to verify the exact number.

COMMENTS

By far the most frequent complication of triplet pregnancy is preterm labor. Aggressive management policies are necessary in order to anticipate the onset of premature labor. Such policies might include cervical assessment by vaginal examination from the 22nd week onward and the use of external monitoring devices to document insensible contractions. In conjunction with these policies, obstetricians must be prepared to institute bed rest and/or tocolysis on short notice. Although no consensus exists regarding the efficacy of bed rest in decreasing premature labor and preterm delivery in triplets, this intervention has little potential risk and offers many potential benefits. In spite of the lack of comparative randomized efficacy trials in triplet gestations, the use of tocolytic agents also logically may be of benefit in prolonging gestation.

Delivery by cesarean section is almost uniformly advocated for certain forms of first-fetus malpresentation in multiple gestations. When fetal malpresentation is not present, however, prior experience, anecdotal recollections and hospital-dependent policies appear to be the most persuasive elements in decisions affecting route of delivery. It is tempting to propose that multicenter randomized controlled studies address this issue; however, the logistics of such an approach and the extremely small number of potential patients to enroll in trials, as well as the adverse medical-legal implications of any outcome judged less than ideal, all speak against the likelihood of such trials ever coming to pass. In contrast, it is reasonable to propose that ultrasound be used more often to aid in the diagnosis of triplet pregnancy and to monitor its management.

The need to develop a more comprehensive data base on triplets as well as higher order multiple births is underscored by the following considerations: 1) fertility-inducing agents are being used with increasing frequency in developing as well as developed nations,

Table 3 - Triplet case reports by year of publication

Ref.	Year	Country	Subject	Zygoty	No. cases
26	1982	USA	Pyloric stenosis	MZ	1
16	1982	USA	Pyloric stenosis	MZ	1
18	1981	USA	Prenatal genetic dx and amniocentesis	TZ	1
43	1984	USA	Congenital toxo- plasmosis	Not stated	
9	1983	UK	Asperger's syndrome	MZ	1
40	1983	USA	Diabetes	MZ	1
28	1985	USA	Conjoined twins	DZ	1
10	1984	N. Zealand	Heterotopic pregnancy	DZ	1
15	1983	Norway	Infantile autism and fragile X-chromo- some	Presumably MZ	1
44	1985	Australia	Goldenhar syndrome	DZ	1
39	1980	Germany	Ventricular fibroelastosis	Presumably MZ	1
32	1983	Jugoslavia	Dental malocclusion	Varied	42
5	1984	USA	Deafness	Presumably MZ	1
19	1982	Japan	Cranio-thoracopagus	MZ	1

and this innovation in all likelihood will lead to more triplet pregnancies. 2) the regionalization of perinatal services throughout the world will increase the survival rate among triplet infants born prior to term.

In order to facilitate acquiring a clinically useful body of knowledge regarding triplet pregnancies and births, the following academic issues should be addressed: 1) the method of presentation of national data should be standardized; 2) clinical data from hospitals and regions should incorporate comments on therapies that are presently in question, ie, the type and dose of tocolytic agents when used, the amount and duration of bed rest, the use of ultrasonography, and methods employed to determine zygosity; 3) the preferred route of delivery, type of anesthesia and cost of care should be described, at a minimum. The complexity and importance of these questions may possibly be best addressed by an international conference convened by the International Society for Twin Studies.

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