CHAPTER V

SPONTANEOUS ABORTIONS IN MOTHERS OF DOWN SYNDROME
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INTRODUCTION

Interest in the reproductive histories of mothers of children with trisomy 21 comes from various sources. First was provided by Ayme and Lippman-Hand (1982). They suggested that there is decreasing selection against pregnancies with an extra autosome or X chromosome with increasing maternal age. Their work refocussed attention on fetal losses in the sibships of index cases. Secondly, there is growing emphasis on the need to identify risk factors for trisomy. So, it is worthwhile to evaluate the extent to which a history of spontaneous abortion might predict the birth of a chromosomally abnormal child.

There is convincing evidence that women with a live born child with trisomy 21 have an increased risk of having another live born child with either the same or different trisomy, particularly when the mother is below 30 years of age when the first affected child is born (Carter and Evans, 1961; Stene, 1970; Richards, 1977). This observation was again confirmed by Mikkelsen and Stene (1979) using data from the European Collaborative Prenatal Diagnosis study. In their analysis of 2643 pregnancies following a Down Syndrome child, Mikkelsen and Stene (1979) reported that women who were under 24 years at the time of birth of index child, had about 6 times the number of affected pregnancies expected. This shows a significantly increased risk for recurrence of trisomic offspring. If this risk is evidence of an increased production of trisomic conceptions, women with an affected child should have higher than average
rate of spontaneous abortion in their pregnancies, since the majority of aneuploid conceptuses will be aborted (Lippman-Hand and Ayme, 1984).

**Spontaneous Abortions and Aneuploidy**

It is seen that the estimated frequency of aneuploidy at conception is far greater than the frequency at birth, as selection of vast majority of aneuploid conceptuses operates prenatally through spontaneous abortions or foetal death in different stages of gestation.

The first cytogenetic studies of consecutive series of human spontaneous abortuses (Carr, 1963; Clendenin and Benirschke, 1963) demonstrated a relatively high incidence of chromosomal anomalies. Since then, many workers have recorded a high incidence of chromosomal abnormalities in spontaneously aborted fetuses, particularly in those aborted in the first trimester. The results from some of the numerous cytogenetic surveys of spontaneous abortions are mentioned.

In the early studies, the overall frequency of chromosome anomalies were 8% (Stenchever et al., 1967), 60% (Boue et al., 1975) or 64% (Szulman, 1965). Creasy et al. (1976) in their study observed 30.5% of the abortuses to be chromosomally abnormal, of which 49.8% were primary autosomal trisomies, 23.7% X monosomies and 17.4% polyploid whereas, Hassold et al. (1978) observed that almost 46.6% of the spontaneous abortus were chromosomally abnormal and almost all of these involved numerical aberrations. In their study, the single most common abnormality was monosomy X accounting for over 10% of all abortions and almost 25% of chromosomally abnormal samples. Autosomal trisomies were observed in 45.9% of the chromosomally abnormal abortuses. Trisomy 16 was the most common, followed by
trisomies 21 and 22.

Kajii et al. (1980) reported that 54% of all recognizable spontaneous abortions are chromosomally abnormal, almost all of these involved numerical aberrations. More than 50% of the abnormal cases were observed to be primary autosomal trisomy, one fifth to be monosomy X and nearly one-seventh to be polyploid. Trisomy 16 was present in 28% of trisomic abortuses followed by trisomy 21 (9%) and trisomy 22 (14%). Hassold and Chiu (1985) observed an overall rate of chromosome abnormality to be 50.4% of spontaneous abortion, with trisomy accounting for nearly 30% of the abortions; and sex chromosome monosomy and polyploidy for approximately 10% each.

Eiben et al. (1987) found abnormal karyotypes in one-half of the spontaneous abortion cases studied by analysing chromosome directly from chorionic villi. Trisomy predominated in their study (≈65%), followed by polyploidy (≈20%), monosomy X (≈10%) and structural anomalies (≈4%). Among trisomies, chromosome 16, 22 and 21 were prevalent.

Chromosome abnormality in trimester-wise pregnancy loss

The actual frequency of chromosome abnormality in spontaneous abortions has varied from one survey to another, and this is due to a number of factors - sample size, selection of sample, maternal age and gestational age of the fetus. According to Bond and Chandley (1983) the most important criterion for selection is gestational age of the fetus at expulsion. Boue et al. (1975) in their sample observed that most of the abortions occurred during the first 3 months of gestation.

Creasy et al. (1976) reported that the proportion of chromosomally abnormal
abortuses decreased with increasing gestational age. They recorded the highest proportion (60%) at 11 weeks, after which it decreased rapidly to less than 20% at 18th week. Kajii et al. (1980) observed similar results, the highest (74%) rate was recorded at 9 weeks after which the rate decreased gradually to 33% by 19-30 weeks. Eiben et al. (1987) noted in their study that chromosome anomalies were highest in abortions of 10-11 weeks of gestation.

Allowing for differences in selection of aborted material and other variables, the overall frequency of chromosome abnormalities and the relative frequencies of different type of abnormality are quite similar. Exception is the study by Creasy et al. (1976) who found an abnormality rate of 30.6% which is much lower to those of other studies. It may be said in general, that approximately 50% of spontaneous abortions are chromosomally abnormal and autosomal trisomy accounts for approximately half of the abnormalities encountered in abortuses. Moreover trisomies of all the groups have been reported. The overall rate of trisomy among abortions is approximately 25%, or some 80 times greater than the rate in new born infants (Hassold and Jacobs, 1984). Eventhough cytogenetic analysis of abortuses represents an improvement over studies on live born infants, chromosome anomalies found in the abortuses still represent only a part of the total that occur at fertilization, as a substantial number of conceptuses may be eliminated very early, even before pregnancy is recognised. Thus, the live born children with chromosomal aberrations constitute only the tip of the iceberg of chromosomally abnormal conceptuses, since chromosomal aberrations, in the overwhelming majority of cases, are not compatible with life.

According to Hassold and Jacobs (1984), the observed incidence of trisomy depends on two factors, the extent of in utero selection and the incidence at
conception. Many attempts have been made to estimate the frequency of chromosome abnormalities and trisomy at the time of conception. Published estimates for the frequency of all chromosomally abnormal zygotes at conception in man range from 8-10% (Alberman and Creasy, 1977), 20% (Ford, 1975) and 50% (Boue et al., 1975). The wide variation in estimates is largely because of different methods used to calculate the figure. According to Bond and Chandley (1983), some human trisomies and virtually all autosomal monosomies are likely to be eliminated very early so that pregnancy is not recognized. Most autosomal monosomies in the mouse are eliminated before implantation (Gropp et al., 1976) and in man although sometimes found among early spontaneous abortions, are rarely recovered. Ford (1981) calculated a frequency of aneuploid human fetuses at the time of clinical recognition of pregnancy to be 8%. As regards trisomy, Boue et al. (1975) reported that approximately 20% of all conceptions were trisomic, almost all of which were presumed to terminate in spontaneous abortion.

Studies of live born individuals suggests that the occurrence of an autosomal trisomy may increase the likelihood of a second trisomy, involving either the same or a different chromosome (Hassold, 1980). Based on earlier studies, Stene (1970) presented evidence indicating that the risk of trisomy 21 is greater for women under 30 years who have already borne a trisomy 21 child than it is for the corresponding general population of the same age group. Further, Hecht (1984) showed an increased frequency of trisomy 21 among siblings of individuals with trisomy 18, and suggested an association between trisomies for different chromosomes. But, data from the live born population regarding the possible relationship among different autosomal anomalies are very few, especially due to elimination of large proportion of
conceptuses carrying chromosomal anomalies during pregnancy as discussed earlier.

Spontaneous abortions are an excellent source of data for evaluating possible associations among chromosome anomalies. Trisomy is found to be common among spontaneous abortions. Unfortunately very scant data exists on the frequency of trisomy found in pregnancies before and after a karyotyped spontaneous abortion with aneuploidy.

Alberman et al. (1975) detected a ten-fold increase in Down Syndrome among live born siblings of trisomic spontaneous abortion. They further noted that this could not be explained by gonadal mosaicism in a parent, since in most of the abortions the additional chromosome was clearly not chromosome 21. Lauritsen (1976) and Kajii and Ferrier (1978) also observed a much higher incidence of trisomy following a trisomic spontaneous abortion than following a chromosomally normal abortion and so concluded that there is a strong possibility for trisomy to recur.

Hassold (1980) in a cytogenetic study of successive abortions observed the chromosome constitutions of the first and second abortion to be highly correlated. Combining these observations with those of previous ones (Alberman, 1975; Boue and Boue, 1973; Lauritsen, 1976; Kajii and Ferrier (1978), Hassold (1980) suggested that certain couples are at an increased risk for either repeated chromosomally normal abortions or for repeated trisomic conceptions. Further, the increased risk of trisomy was not observed to be restricted to a particular chromosome.

In the past, there have been a few reports on the frequency of spontaneous abortion in mothers of DS and its role as an increased risk to have a trisomic child. Some studies have reported increased rates of abortion in mothers of DS (Ingalls et al., 1957; Benda et al., 1960; Coppen and Cowie, 1960) while others have proved it
to be wrong (Sigler et al. 1967; Buck et al., 1966).

Increasing maternal age in trisomy 21 children has been observed irrespective of the extra chromosome being of maternal or paternal origin. Further Ayme and Lippman-Hand (1982) suggested that the increasing risk with maternal age for trisomy among live births may be due, at least in part, to a decreasing probability of aborting trisomic conceptions with increasing age.

Hook and Cross (1983) from the trends in their data, concluded that young mothers with more number of spontaneous abortions are at higher risk of a Down Syndrome live birth compared to the women of same age with no previous abortion. Lippman-Hand and Ayme (1984) suggested that women under 25 years at the birth of a Down Syndrome child have a significantly higher rate of spontaneous abortion in their prior pregnancies in comparison to women who delivered the trisomic child at older ages.

In the present study, the reproductive histories of mothers of DS and control mothers have been investigated. The spontaneous abortion frequencies are analysed with the risk of a subsequent birth of aneuploid child, as majority of spontaneous abortions with chromosomal cause are due to aneuploidy.

MATERIALS AND METHODS

Mothers of DS Children

During the period of study, Down Syndrome cases were referred from Ahmedabad city and adjoining areas. 149 clinically suspected Down Syndrome cases were confirmed cytogenetically to be having free trisomy 21. Only mothers of these children with free trisomy 21 were included in the study. Mothers who gave birth to
translocation DS were excluded from the study. All the mothers included in the present study gave birth to a single live born trisomy 21 child.

Control Mothers

One hundred control mothers consisted of volunteer mothers. These mothers did not have any history of birth of trisomic child or any family history of birth of a child with any other chromosomal aberrations which might contribute for spontaneous abortions.

Data Collection

Reproductive histories of each woman was entered in detail in the standard proforma when the families were referred for cytogenetic diagnosis and counselling. With the exception of those terminated by induced abortion, all the recognised pregnancies i.e. both spontaneous abortions and pregnancies resulting in live born children, both before and after the birth of index cases were considered. It was also recorded whether spontaneous abortion in both the groups occurred in the first, second or third trimester of gestation. Further, maternal and paternal ages at the time of each recognised pregnancy was also noted.

Data Analysis

In both the groups, the rate of spontaneous abortions was obtained by analysing the total number of pregnancies by number of spontaneous abortion. The occurrence of spontaneous abortion was also analysed according to trimester-wise fetal loss. Incidence of pregnancy loss was analysed with respect to maternal age group (≤ 20,
The rate of spontaneous abortions prior and subsequent to the birth of index child was also determined. The data was analysed using Student's 't' test.

Results

All the 149 mothers of DS had given birth to a single live born child with free trisomy 21.

Spontaneous abortion Rates in Control and Mothers of DS

Table 26 summarizes the reproductive history of controls and mothers of DS. The control mothers were observed to have a total of 310 pregnancies with a mean pregnancy of 3.1. Mothers of DS had a total of 479 pregnancies with a mean pregnancy rate of 3.2. Thus, the mean conception rate of both groups did not vary significantly. While the controls lost 23 pregnancies in spontaneous abortions, the mothers of DS had a total of 82 fetal losses. With respect to the frequency of spontaneous abortions, 7.41% pregnancies ended as spontaneous abortion in controls, and 17.11% were lost as spontaneous abortions in mothers of DS. This value was statistically significant for mothers of DS in comparison to pregnancy loss in control mothers (P<0.02).

Spontaneous Abortion according to each Trimester

The occurrence of spontaneous abortions in relation to each trimester is given in Table 27 and in Fig.XXVII. As can be noted from the table, in both the groups the majority of spontaneous abortions occurred in the first trimester of pregnancy. In
controls out of the total of 23 abortions, 14 occurred in first-trimester, 7 in second trimester and 2 in third trimester, while, in mothers of DS 63 abortions occurred in first trimester, 17 in second trimester and 2 in third trimester. The spontaneous abortion frequency in first trimester was significantly higher in mothers of DS as compared to control mothers (P<0.02); the values were not significant for second and third trimester.

### Spontaneous abortions and Maternal age

The data for spontaneous abortion in controls and mothers of DS according to maternal age at the time of each pregnancy is presented in Table 28. In both the controls and mothers of DS, the highest number of pregnancies occurred in the maternal age group of 21-30 years.

For the control mothers and mothers of DS maximum abortion occurred during the age group of 21-25 and 26-30 years. In controls, no pregnancy loss occurred below 20 years while in mothers of DS, 4 cases of abortion had occurred. In the age group of 36 and higher, 3 abortions occurred in controls while mothers of DS did not experience any fetal loss, although in this age group, out of total of 27 pregnancies, 15 Down Syndrome children were born. The data of spontaneous abortion cases according to maternal age is presented in Fig.XXVIII.

The occurrence of spontaneous abortions in mothers of DS, preceding and subsequent to the birth of Down Syndrome child with respect to maternal age is shown in Table 29 and Fig.XXIX. 22.7% pregnancies ended as spontaneous abortions preceding the birth of DS child, while 9.1% pregnancies were lost subsequent to the birth of DS child. The total rate of pregnancy loss was significantly higher (P<0.01)
Table 26

Summary of reproductive history in controls and mothers of DS

<table>
<thead>
<tr>
<th>DATA</th>
<th>CONTROL</th>
<th>MOTHERS OF DS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of mothers investigated</td>
<td>100</td>
<td>149</td>
</tr>
<tr>
<td>No. of DS birth</td>
<td>-</td>
<td>149</td>
</tr>
<tr>
<td>No. of clinically recognised pregnancies</td>
<td>310</td>
<td>479</td>
</tr>
<tr>
<td>Mean pregnancy rate</td>
<td>3.1</td>
<td>3.2</td>
</tr>
<tr>
<td>Total No. of abortions</td>
<td>23</td>
<td>82</td>
</tr>
<tr>
<td>Percent abortions</td>
<td>7.41</td>
<td>17.11*</td>
</tr>
</tbody>
</table>

*P<0.002
**Table 27**

Distribution of spontaneous abortions in controls and mothers of DS in Relation to each trimester

<table>
<thead>
<tr>
<th>Group</th>
<th>Total No. of pregnancies</th>
<th>No. of live births</th>
<th>Spontaneous Abortion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1st trimester</td>
</tr>
<tr>
<td>Control</td>
<td>310</td>
<td>287 (92.5%)</td>
<td>14 (4.52%)</td>
</tr>
<tr>
<td>Mothers of DS</td>
<td>479</td>
<td>397 (82.8%)</td>
<td>63 (13.15%)*</td>
</tr>
</tbody>
</table>

* P<0.02
TRIMESTER WISE SPONTANEOUS ABORTIONS

* P<0.02
Table 28

Spontaneous abortion according to maternal age in control and mothers of DS

<table>
<thead>
<tr>
<th>Maternal age (years)</th>
<th>No. of pregnancies</th>
<th>Control</th>
<th>Spontaneous abortion (%)</th>
<th>Spontaneous abortion (%)</th>
<th>Mothers of DS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>13</td>
<td>31</td>
<td>0 (0.00)</td>
<td>31 (12.9)</td>
<td></td>
</tr>
<tr>
<td>21-25</td>
<td>88</td>
<td>178</td>
<td>8 (9.09)</td>
<td>31 (17.4)</td>
<td></td>
</tr>
<tr>
<td>26-30</td>
<td>92</td>
<td>168</td>
<td>8 (8.69)</td>
<td>35 (20.8)</td>
<td></td>
</tr>
<tr>
<td>31-35</td>
<td>62</td>
<td>75</td>
<td>4 (6.45)</td>
<td>12 (16)</td>
<td></td>
</tr>
<tr>
<td>&gt;36</td>
<td>55</td>
<td>27</td>
<td>3 (5.45)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>310</td>
<td>479</td>
<td></td>
<td></td>
<td>82 (17.1)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16.4±15.8</td>
</tr>
</tbody>
</table>
AGEWISE SPONTANEOUS ABORTION CASES

Fig XXVIII

SA as %age of PREGNANCIES

MATERNAL AGE GROUP

< = 20 YRS 21-25 YRS 26-30 YRS 31-35 YRS > = 36 YRS

CONTROL
MOTHERS OF DS
Spontaneous abortions in mothers of DS prior and subsequent to birth of index child

<table>
<thead>
<tr>
<th>Maternal age (years)</th>
<th>Prior to birth of index child</th>
<th>Subsequent to birth of index child</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of pregnancies</td>
<td>Spontaneous abortion (%)</td>
</tr>
<tr>
<td>≤20</td>
<td>22</td>
<td>18.18 (4)</td>
</tr>
<tr>
<td>21-25</td>
<td>120</td>
<td>20 (24)</td>
</tr>
<tr>
<td>26-30</td>
<td>95</td>
<td>27.3 (26)</td>
</tr>
<tr>
<td>31-35</td>
<td>36</td>
<td>27.7 (10)</td>
</tr>
<tr>
<td>&gt;36</td>
<td>8</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>281</td>
<td>22.7 (64)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>12.8±11.7</td>
<td></td>
</tr>
</tbody>
</table>
SPONTANEOUS ABORTIONS
PRIOR & SUBSEQUENT TO THE BIRTH OF INDEX CHILD

Fig XXIX

%age OF TOTAL NO. OF PREGNANCIES

MATERNAL AGE

PRIOR TO INDEX CHILD

SUBSEQUENT TO INDEX CHILD
Table 30

Incidence of trisomy and spontaneous abortions among clinically recognised pregnancies in mothers of DS

<table>
<thead>
<tr>
<th>Maternal age (Years)</th>
<th>% abortion</th>
<th>% trisomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 20</td>
<td>12.9</td>
<td>25.8</td>
</tr>
<tr>
<td>21-25</td>
<td>17.4</td>
<td>24.1</td>
</tr>
<tr>
<td>26-30</td>
<td>20.8</td>
<td>29.1</td>
</tr>
<tr>
<td>31-35</td>
<td>16</td>
<td>45.3</td>
</tr>
<tr>
<td>36-40</td>
<td>0</td>
<td>54.1</td>
</tr>
<tr>
<td>Above 41</td>
<td>0</td>
<td>66.6</td>
</tr>
<tr>
<td>Total</td>
<td>17.1</td>
<td>31.1</td>
</tr>
</tbody>
</table>
MATERNAL AGE & INCIDENCE OF TRISOMY

Fig XXX

MATERNAL AGE

%age OF TRISOMY/SA

ABORTION
TRISOMY

MATERNAL AGE

ABOVE 41

MATERIAL AGE

%age OF TRISOMY/SA

ABORTION
TRISOMY

MATERNAL AGE

ABOVE 41
prior to the birth of DS child as compared to the value subsequent to the birth of index child.

Table 30 and Fig.XXX presents the data of the incidence of abortions and trisomy 21 offspring according to the different age groups in mothers of DS. Taking into account the clinically recognised pregnancies, it is clear from the table that with increasing maternal age, as the incidence of abortions decreases, the incidence of trisomy increases so much so, that in the age group of 36 to 40 years and above 41 years, no spontaneous abortion was reported though 54.1% and 66.6% of the pregnancies resulted in a trisomic offspring respectively.

DISCUSSION

As mentioned earlier, it has been reported that about 50% of spontaneous abortions are chromosomally abnormal and autosomal trisomy accounts for approximately half of these abnormal abortuses (Boue et al., 1975; Kajii et al., 1980; Hassold and Chiu, 1985). Hassold (1980) had indicated that certain couples are at an increased risk for either repeated chromosomally normal abortions or for repeated trisomic conceptions. It was further added that the increased risk of trisomy did not seem to be restricted to a particular chromosome.

Based on their observations that the complements of successive abortuses by a given woman are more likely to be either recurrently normal or recurrently abnormal, Warburton et al. (1987) suggested that aneuploidy may be responsible for recurrent as well as sporadic losses. Abortuses in a given family thus show non-random distribution with respect to chromosomal complements. If the complement of the first abortus is abnormal, the likelihood is 80% that the complement of second
abortus also will be abnormal. The recurrent abnormality usually is trisomy, but it may be monosomy or polyploidy (Simpson, 1993).

Alberman et al. (1975) detected a ten fold increase in Down Syndrome among live born siblings of trisomic spontaneous abortions. They could not explain this observation by gonadal mosaicism in a parent, since in most of the abortions the additional chromosome was not chromosome 21. Boue and Boue (1973) showed in their study of repeated spontaneous abortions that three-fourths of all abortions occurring in women with a previous trisomic abortion were also trisomic. Several workers have reported that women who gave birth to a live born child with trisomy 21 are at an increased risk of having another live born child with either the same or a different trisomy. This was observed particularly when the mother was under 30 years when the first affected child is born (Carter and Evans, 1961; Stene, 1970; Richards, 1977; Mikkelsen and Stene, 1979).

From the above it is clear that some individuals are at risk for an increased production of trisomic conceptions. These reports suggest that certain couples are predisposed towards chromosomally abnormal conceptions, most of which naturally result in spontaneous abortion. If couples were predisposed to recurrent aneuploidy, they might logically be at increased risk for aneuploid liveborns. So, the trisomic autosome in a subsequent pregnancy might not lead to lethality but might be compatible with life (e.g. trisomy 21). Several studies hint that the risk of live born trisomy 21 following an aneuploid abortus is about 1% (Alberman, 1981).

Few investigators had examined the question of increased spontaneous abortions in mothers of DS in the 1950s and 1960s, but the results of these studies have been inconclusive. In some investigations, increased abortion rates have been
observed (Smith and Record, 1955; Ingalls et al., 1957) while in others not (Sigler et al., 1967). Buck et al. (1966) were amongst the first to base a search for alterations in the reproductive characteristics of mothers of children with DS and pointed out that there was no overall difference in losses between 110 mothers of DS cases and 100 control mothers, while Beer et al. (1990) reported a significant higher frequency of spontaneous abortions in mothers of DS.

Lippman-Hand and Ayme (1984) have argued that most of the past investigations which failed to document a major increase over the control population were either too small to be able to detect a difference; or they lacked cytogenetic confirmation of the clinical diagnosis of Down Syndrome; or else they used different methods to obtain reproductive histories from cases and from controls, or they did not analyse 'young' and 'old' case mothers separately. Similarly, Hook and Cross (1983) have suggested that the earlier studies were designed differently, for other purposes and did not have sufficient data on controls. Further, there appears to be discrepancy between these older reports showing no increase in spontaneous abortions, and reports of an increased risk for a trisomic live birth among women who have already had one such affected child (Carter and Evans, 1961; Richards, 1977). Studies of women undergoing prenatal diagnosis supported the general observation that those under 25 years at the birth of a trisomic child appear to have about 1% risk of recurrence in other pregnancies (Mikkelsen and Stene, 1979).

In the present study, the frequency of spontaneous abortions observed in mothers of Down Syndrome (17.11%) was significantly higher than that of controls (7.41%). The observed higher rates of pregnancy loss in mothers of DS in the present study is in line with the reports of others (Lippman-Hand and Ayme, 1984; Beer et
The frequency of spontaneous abortion at different gestational age varies considerably and there is a negative relationship between gestational age and frequency of chromosomal anomaly in spontaneous abortions. A number of studies have reported that most of the chromosomally abnormal pregnancies are lost in the first trimester, at about ten weeks of gestation (Boue et al., 1975; Creasy et al., 1976; Kajii et al., 1980; Hassold and Jacobs, 1984). In the present study, mothers of DS reported 63 abortions in the first trimester out of total of 82 abortions. These significantly higher frequency of spontaneous abortions in mothers of DS in first trimester suggests an increased risk of having trisomic pregnancies as indicated by the previous works on spontaneous abortions. In controls no abortion was reported below 20 years, whereas, in mothers of DS, 12.9% of pregnancies were lost in abortion. In subsequent age groups of 21-25, 26-30, 31-35 and ≥36 years, the fetal loss rate was more or less similar in the controls but in mothers of DS it was highest in the age group of 26-30 years, followed by 21-25 years and 31-35 years. Moreover, in the above 36 age group, no spontaneous abortion was reported in mothers of DS, though more than half of the pregnancies (55.5%) resulted in live born trisomy 21 child. These observations are in accordance with the conclusion of Ayme and Lippman-Hand (1982) that in older women the ability to selectively abort aneuploid fetuses is decreased. Similarly, Hook and Cross (1983) reported from their data that younger the women and more the number of abortions, the higher is the relative risk of Down Syndrome live birth compared to the rates for women of same age with no previous abortion. Women under 25 years at the birth of the trisomic child have a significantly higher rate of fetal loss in their pregnancies as compared to those who delivered the trisomic child at
older ages (Lippman-Hand and Ayme, 1984). It is known that mothers of DS who were less than 35 years had significant increase in the rate of spontaneous abortions (Beer et al., 1990).

Very few studies have been carried out on the frequency of spontaneous abortions prior and subsequent to the birth of the index child in mothers of DS. Sigler et al. (1967) observed significant increase in the rate of multiple miscarriages prior to the birth of the index children as compared to controls. Lippman-Hand and Ayme (1984) reported that the rates of spontaneous abortion prior to the birth of the proband was significantly higher in mothers of DS at age 20-24 years, while the rates of prior loss in all the other subgroups were fairly similar. In the present study, when the rates of spontaneous abortions prior to the birth of index child were compared to those subsequent to the birth of this child, a significant increase was observed in the frequency of spontaneous abortions prior to the birth of index child in all the age groups except the above 36 years group. This significant increased rate of spontaneous abortions in mothers of DS prior to the birth of index child might indicate the risk for having an aneuploid child, including trisomy 21.

In conclusion, the observations in the present study are in accordance with the reports of Hook and Cross (1983), Lippman-Hand and Ayme (1984) and Beer et al. (1990). From this data, it is observed that mothers of DS had higher frequency of spontaneous abortions, particularly below 35 years of age and majority of these abortions occurred during the first trimester of pregnancy. Further, most of the abortions were observed prior to birth of the DS child and no fetal loss was reported by mothers of DS in the above 36 years age. However, the suggestions are preliminary and more data are needed to determine the explanation of the observations made and
its implication for genetic counselling - the extent to which a history of spontaneous abortion may be used to predict the birth of a chromosomally abnormal child.
A conclusion is a place where you get tired of thinking.

- Murphy’s Law