Repeated successful pregnancies after kidney transplantation in 102 women (Report by the EDTA Registry)*


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Abstract

Background. Between 1967 and 1990, 820 successful pregnancies in 718 women on renal replacement therapy (RRT) were reported to the EDTA Registry.

Methods. This study analyses data on repeated successful pregnancies in 102 of these women, of whom 99 had two and three had three pregnancies.

Results. Primary renal diseases were mainly glomerulonephritis (41%), pyelonephritis (32%), and congenital malformations such as cystic diseases and hypoplasia or dysplasia (13%). Mean age at start of RRT was 21 years ± 5 SD. Ninety-four per cent of the women had the same transplant during the first and second pregnancies; 85% of these were alive with their first graft and 9% with a second graft; 4% were retransplanted after the first pregnancy and 2% were back on dialysis during the second pregnancy.

Of the mothers with two successful pregnancies, two-thirds had a serum creatinine below 121 μmol/l after the first or after the second pregnancy. Six mothers lost their first graft after the first pregnancy. None of the mothers had died after delivery of the second or third baby.

Several features of the first and the second pregnancy in these mothers were quite similar. Mean gestational age was 36 weeks ± 3 SD during first and second pregnancy. Mean birth weight (height) of the first child was 2490 g ± 660 SD (48 cm ± 4 SD) and 2587 g ± 639 SD (50 cm ± 3 SD) of the second child (NS). Neonatal mortality was 4% after the first and second delivery; congenital abnormalities were found in five and three children respectively.

Conclusions. Fourteen per cent of mothers who had a successful pregnancy on RRT subsequently had a second baby. Repeated pregnancies should not adversely affect graft function and/or fetal development provided that graft function was well preserved at the time of conception.

Key words: renal transplantation; pregnancy; newborns

Introduction

More than 100 reports have been published in the international literature concerning pregnancies in women after renal transplantation. Most were based on single-centre experiences with less than 50 cases. Few studies have summarized multicentre data on larger numbers of pregnancies [1-6]. Since 1977 the EDTA Registry has been writing annually to clinicians in Europe, and by 1990 had gathered information on 820 successful pregnancies reported from 2541 dialysis and transplant centres [4,7-9]. This study reports data on repeated successful pregnancies after kidney transplantation in 102 of these women. Information is given on graft function, gestation, and on the clinical status of the first and second newborn.

Subjects and methods

In 1978 a detailed questionnaire was sent by the EDTA Registry to the centres asking retrospectively for details of each pregnancy reported before 31 December 1977. Since then special questionnaires have been sent annually to each centre reporting one or more babies born to mothers on RRT on the yearly centre questionnaire. The contents of the questionnaires and the methods of data collection have previously been described [4,10].

Results

Among the 718 reported women delivering a live child on RRT between 1967 and 1990 were 102 mothers (14%) who had repeated successful pregnancies. Of these women, 99 mothers had two and three had three
successful pregnancies on RRT. Ninety-four per cent had the same transplant during the first and second pregnancies: 85% of these were their first graft and 9% their second graft. Four per cent were retransplanted after the first pregnancy and 2% returned to dialysis at the end of the second pregnancy. Seventy-eight per cent of mothers with a first transplant were alive with a cadaveric donor graft and 22% with a live donor graft.

The distribution of primary renal diseases amongst transplanted women having repeated pregnancies were glomerulonephritis (41%), pyelonephritis (32%), and congenital malformations (13%) and other (14%) (Figure 1).

The mean age of these women was 21 years ±5 SD at start of RRT, 23 years ±5 SD at first transplantation and 27 years ±5 SD at the time of first delivery. Fifty per cent of mothers experienced their second successful pregnancy within 2 years of the first delivery.

Of 56 mothers for whom information on immunosuppression was available, 90% received azathioprine continuously during the first and second pregnancy and 10% were on continuous cyclosporin A.

Since documentation of serum creatinine codes was not introduced until 1985, data on graft function during second pregnancy was reported in only 34 women. Twenty-three (70%) of these mothers had a serum creatinine below 121 µmol/l in the year of delivery, three between 121 and 160 µmol/l, five between 161 and 200 µmol/l, and three between 201 and 240 µmol/l. Two of the 102 mothers had returned to dialysis during the second pregnancy and four were retransplanted before the second pregnancy.

Repeated live births were reported from the following countries: the United Kingdom 50, France 21, Belgium and Spain 7, Germany and Sweden 4, Italy, Finland and Denmark 2, and one each in Czechoslovakia, Norway, and Greece.

The mean duration of gestation for babies born to women on RRT was 36 weeks and thus shorter than in the normal population and did not differ between the first and second pregnancy (Table 1). Mean birth weight, height, and head circumference were lower than in the normal population. Differences of birth weight, body height, and head circumference between the first and second babies were minor, with slightly higher values in the second child (Table 1).

Congenital malformations were found in five of the first-born babies and in three offspring of the second pregnancy (Table 1). The congenital malformations reported were oesophageal atresia, plagiocephaly with delayed statomotor development, nephronophthisis, hydronephrosis, posterior urethral valve, hypospadias, and club foot; congenital malformations were not specified in one child. One mother gave birth to a first child with oesophageal atresia and to a second child with hypospadias.

Neonatal mortality within the first 4 weeks was 4% in both the first and second child (Table 1). Neonatal death occurred mostly in very small infants and was attributed to prematurity. For comparison, neonatal mortality in 669 first children reported to EDTA to be born to mothers on RRT (90% transplanted, 10% dialysed) was 3.4% and was related to gestational age (Figure 2), method of renal replacement therapy and transplant function (Table 2).

Table 1. Outcome of first and second pregnancy in 102 transplanted women (mean values and standard deviation)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1st pregnancy</th>
<th>2nd pregnancy</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (weeks)</td>
<td>36 ± 5</td>
<td>36 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2490 ± 660</td>
<td>2587 ± 639</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>48 ± 4</td>
<td>50 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>33 ± 3</td>
<td>34 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td>Neonatal mortality (%)</td>
<td>4.0</td>
<td>3.6</td>
<td>NS</td>
</tr>
<tr>
<td>Congenital malformations (%)</td>
<td>5</td>
<td>3</td>
<td>NS</td>
</tr>
</tbody>
</table>
Successful pregnancies may represent a selection of women on the psychosocial situation of these mothers, especially having undergone medical care, psychological counselling, and life experience during their first pregnancy. Unfortunately we were unable to obtain information to avoid unnecessary complications and deceptions.

Transplanted women of childbearing age is warranted to revise their views. It seems prudent to discuss actively the possibility of having repeated pregnancies. Makowski and Penn published four and five repeated pregnancies after transplantation in two women. We recognize that pregnancy in a transplanted woman is not without risk. Careful counselling of transplanted women of childbearing age is warranted to avoid unnecessary complications and deceptions.

Our reported group of mothers with repeated successful pregnancies may represent a selection of women who have planned at least their second pregnancy after having undergone medical care, psychological counselling, and life experience during their first pregnancy. Unfortunately we were unable to obtain information on the psychosocial situation of these mothers, especially on those six mothers who lost their first graft after giving birth to a first child and still had another pregnancy. Our analysis was based on the patient questionnaires and mini-questionnaires of the EDTA Registry which contain a limited amount of information, e.g. causes of graft failure and long-term survival of newborns could not be analysed. Furthermore the extent of underreporting remains unclear. In general, three-quarters of centers report on their patients regularly. It may be argued that the data presented could have been biased by the method of collection and that the good results were due to the fact that patients were selected. In fact our study analysed successful pregnancies only and the number of spontaneous abortions or interruptions were not reported.

EDTA data based on 820 successful pregnancies between 1967 and 1990 showed that neonatal mortality was basically related to prematurity and was only slightly higher than in a control group of newborns matched for gestational age [17]. Effective control of arterial hypertension in women with underlying renal disease resulted in fetal survival rising from 55 to 94%, which was in the range of a healthy control group [13]. Thus, women with stable and well-preserved graft function, in the absence of severe hypertension [18] and other risk factors such as genetic defects have an approximately 92–95% chance of delivering a healthy child if pregnancy is not terminated by an abortion. It should be remembered that babies of transplanted mothers have a minimally increased risk of developing congenital malformations or intrauterine growth retardation [4,6]. Azathioprine, and probably also cyclosporin A, had no major teratogenic effect [4,9,19,20].

Several studies have come to the conclusion that grafted mothers might suffer from severe damage to the graft during pregnancy [14,21]. However, other studies including the data from the EDTA Registry have found that pregnancy could be considered to be relatively safe in women with a hitherto well-functioning graft [4,12,22–25]. A case-controlled study with a post-transplant follow-up for a mean of 12 years [20] found no adverse effect of pregnancy on long-term renal function. Decline of graft function was no greater in 53 transplanted mothers than in the matched control group [4]. One mother has had five pregnancies and one abortion after transplantation without deterioration of graft function [16]. Our data on repeated pregnancies reveal that the mean gestational age, birth weight, height and head circumference of the second child was equal or slightly higher than in the first child. This indicates that transplant function, which influences birth weight of the fetus, did not decrease substantially in these mothers with two successful pregnancies. Graft failure rate has been low both during and after successful pregnancy. Of 53 graft losses in 718 women with a successful pregnancy, only one occurred during pregnancy, 11 during the first year after birth of the child, and 41 after 1–9 years [9].

No maternal death was reported after delivery of the second child. However, a maternal death rate
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analysis was not possible because of the lack of a suitable control group. A previous study has shown that death occurred more than 3 years after pregnancy in two-thirds of 21 mothers who were reported to have died after pregnancy [9]. Only three mothers died during the first year postpartum and the causes of death were not different from other women of childbearing age. The life risk of a transplanted woman during successful pregnancy remains to be quantified in large study populations, being the only way to avoid individual bias.

References


Received for publication: 30.1.95
Accepted in revised form. 21.3.96