Arab Journal of Urology (2012) **10**, 175–181

Arab Journal of Urology
(Official Journal of the Arab Association of Urology)

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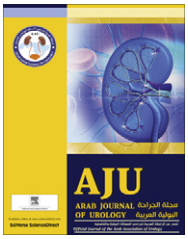

RENAL/TRANSPLANTATION

REVIEW

Pregnancy in renal transplantation: Recipient and donor aspects in the Arab world

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Received 13 December 2011, Received in revised form 17 February 2012, Accepted 18 February 2012
Available online 4 April 2012

KEYWORDS

Fertility;
Immunosuppression;
Side-effects

ABBREVIATIONS

ESKD, end-stage kidney disease; KDIGO, kidney disease: improving global outcomes; CMV, cytomegalovirus

Abstract ***Objective:*** There are many kidney transplant recipients and living donors of reproductive age, and the prevalence of pregnancies in kidney transplant recipients can reach 55% in the Middle Eastern countries. Living kidney donation is predominant in this region. As the risks and outcomes of pregnancy should be a part of counselling for both recipients and donors, we reviewed available reports on maternal and foetal outcomes in these particular populations.

Methods: Information was obtained from retrospective analyses of a large database, and from single-centre reports indexed in PubMed on pregnancy in donors and kidney transplant recipients. The keywords used for the search included 'fertility', 'kidney disease', 'pregnancy', 'maternal/foetal outcomes', 'kidney transplant recipient', 'immunosuppression side-effects', 'living donor' and 'Arab countries'.

Results: Pregnancies in kidney transplant recipients are most successful in those with adequate kidney function and controlled comorbidities. Similarly to other regions, pregnant recipients in the Middle East had a higher risk of pre-eclampsia (26%) and gestational diabetes (7%) than in the general population. Caesarean section was quite common, with an incidence rate of 61%, and the incidence of pre-term birth reached 46%.

Conclusions: Most living donors can have successful pregnancies and should not be routinely discouraged. Women who had pregnancies before and after donation

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Peer review under responsibility of Arab Association of Urology.
http://dx.doi.org/10.1016/j.aju.2012.02.004

Production and hosting by Elsevier

were more likely to have adverse maternal outcomes (gestational diabetes, hypertension, proteinuria, and pre-eclampsia) in the latter, but no adverse foetal outcomes were found after donation. The evaluation before donation should include a gestational history and counselling about the potential risks.

Introduction

End-stage kidney disease (ESKD) negatively affects fertility due to hypothalamic-pituitary suppression, resulting in abnormal or even cessation of menstruation in most pre-menopausal women [1,2]. The incidence of pregnancy in patients on haemodialysis is $<1\%$ to $\approx 7\%$ [3–7], but an improvement in conception rates to 15.9% was reported in patients on nocturnal dialysis [8]. The pregnancy rate on peritoneal dialysis was reported to be even lower (1.1%), possibly due to hypertonic solution causing damage to the Fallopian tubes or interference with ovum transport from the ovaries to the Fallopian tubes [7]. Pregnancies in patients on dialysis are associated with significant risks, including hypertension (67%), pre-eclampsia (19%) and polyhydramnios (40%). Foetal outcomes are adversely affected, with an increased incidence of pre-term delivery, lower gestational age and birth weight, especially in women with pre-eclampsia [9]. Successful kidney transplantation leads to restoration of fertility, with pituitary-gonadal hormone levels returning to the normal range as early as 3–4 months after transplantation. Moreover, both men and women report an improvement in libido and sexual function [10].

Pregnancies in women with a solitary kidney have been previously described and are not contraindicated, although there is a known association between the native kidney disease and adverse maternal/fetal outcomes [11,12]. Many studies suggested that an elevated creatinine level of >1.5 mg/dL is associated with pre-term delivery, increased risk of graft loss, low weight birth and increased incidence of Caesarean section in kidney transplant recipients [13,14]. Those results stem the concern about the potential effect of a reduced GFR on pregnancy in kidney transplant recipients and their donors. The first encouraging results on pregnancy in transplantation came from the recipient-donor pair, Edith and Wanda Helm. After receiving a kidney transplant from her sister in 1956, Edith later gave birth to two healthy babies. The donor, Wanda, gave birth to four healthy babies after donation [15]. Edith died from causes unrelated to transplantation at the age of 76 years on 4 April 2011, as the world's longest surviving kidney transplant recipient.

The Helm sisters were the first examples of many other encouraging results that contributed to allowing pregnancies in transplant recipients and their donors. Recipients and donors of reproductive age seek advice about potential maternal/fetal complications related to the reduced nephron mass and long-term health after pregnancy. Increasing reports contribute to understanding the potential maternal/fetal risks and facilitate counseling by the physician of these populations both before and after conception.

Kidney transplant recipients

The number of female kidney transplant recipients of reproductive age has been steadily increasing, and many look forward to starting a family after the transplant. While the optimum interval between the transplant and conception has not been well determined, the American Society of Transplantation and the National Transplantation Pregnancy Registry group [16,17], as well as 'Kidney Disease: Improving Global Outcomes' (KDIGO) guidelines (2009) [18] recommend waiting at least 1 year after the transplant, to allow for the stabilisation of kidney function and to minimise the risks to mother and fetus. Recipients should be on a stable immunosuppression regimen and should have no active infections or acute rejection episodes in the preceding year. Special considerations should be given to potential mothers of advanced age, suboptimal kidney allograft function and those with multiple comorbidities that might compromise the pregnancy outcomes, as well as recipients with rejection episodes in the first year after transplantation and a history of medical noncompliance. Maternal fetal specialists well versed in the special needs of kidney transplant recipients should be involved early in the management of the potential mother, ideally before she conceives.

The potential teratogenicity of commonly used immunosuppressants should be thoroughly discussed, with an understanding that the comprehensive data on the safety and pharmacokinetics of immunosuppressants in pregnancy are not adequate [19]. Reclassified by the USA Food and Drug Administration from a category C (adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well) to D (studies in humans or investigational or post-marketing data have shown fetal risk), mycophenolate mofetil should be discontinued at least 6 weeks before pregnancy, as it has been shown in case reports and registry data to cause fetal malformations, with the distinctive and unique phenotypes of

ear, mouth, finger and ocular/organ involvement [20]. Although there are some concerns from the association of azathioprine use with fetal abnormalities in animals, most practitioners consider this medication a safe alternative, based on its long record of use in transplant recipients. Azathioprine and corticosteroids both have little to no evidence of teratogenic risk. Although calcineurin inhibitors can cross the placenta, and have been previously shown to have immunosuppressive properties in fetal blood, the USA registry data have shown no pattern of congenital anomalies associated with these agents, and both cyclosporin and tacrolimus are usually continued during the pregnancy [21]. Data on the safety profile of sirolimus and everolimus are limited, and both are currently classified as category C and should be stopped before conception, as per the KDIGO guidelines [18].

Maternal risks

Medical optimisation of comorbidities is essential to increase the success of pregnancy for both mother and fetus. The prevalence of comorbidities is much higher than in the general population, which might be related to the pre-existing kidney disease and immunosuppression. Up to 70% of recipients can develop hypertension before conception [22], which is associated with intrauterine growth retardation, pre-term delivery, miscarriages and low birth rate [23]. Thus, optimising blood pressure control before conception is prudent. Foetotoxic antihypertensive agents (e.g. angiotensin-converting enzyme inhibitors) should be avoided and replaced, if necessary, with alternatives with proven safety records, including α-methyldopa, nifedipine, labetalol and hydralazine [24]. Blood pressure during pregnancy should be maintained close to normal [18]. In many recipients proteinuria in late gestation is due to increased protein filtration, which can exceed tubular re-absorptive capacity [25], but excessive proteinuria might require a kidney biopsy, which should not be delayed until after the pregnancy. Diabetes is yet another highly prevalent comorbidity, with a potential negative effect on pregnancy outcomes. About 30% of recipients are diagnosed with diabetes at the time of transplantation, and another 15% can develop new-onset diabetes after transplantation [26]. Preconception care should include optimising the management of diabetes. The risk of maternal infections is increased due to ongoing immunosuppression. UTIs are common, with an incidence as high as 40% [6]. Physiological hydronephrosis can be present in two-thirds of women, and increases the risk of urinary reflux and subsequent pyelonephritis [27,28]. For an early diagnosis, urine should be analysed and cultured at every prenatal visit. Treatment, preferably with penicillin or cephalosporin, is typically necessary to avoid maternal and fetal complications [29]. While impairment of graft function due to hydronephrosis is rare, ultrasonography of the transplanted kidney should be a part of the evaluation for graft dysfunction, and appropriate management of obstruction with a ureteric stent or nephrostomy tube is recommended [30].

The risk for opportunistic infections in the transplant recipient is relatively high. One of the most common is cytomegalovirus (CMV), which can be transmitted with the transplanted organ or reactivate in women on maintenance immunosuppression. Infection typically occurs in the first few months after transplanting, but the delay in onset is possible due to the common use of CMV prophylaxis [31]. CMV infection *in utero* carries the risks of fetal abnormalities, including microcephaly, intracranial calcifications, growth restriction and others, especially seen in women not previously exposed to CMV. Valganciclovir is the treatment of choice for the CMV infections, but its efficacy is unknown in pregnancy. The other opportunistic infections associated with the adverse fetal outcomes include herpes simplex virus and toxoplasmosis [32].

The management of other comorbidities, related to pre-existing ESKD, suboptimal kidney allograft function and the side-effects of immunosuppressants, should be optimised. Osteopenia, osteoporosis and bone fractures are significantly more prevalent in transplant recipients than in the general population. Vitamin D deficiency is common, and supplements should be initiated ideally before conception, unless contraindicated. Anaemia is highly prevalent in the antenatal period, and can affect up to 25% of pregnant women. While dilutional anaemia occurs due to the disproportional increase in plasma volume compared to red blood cells, iron deficiency is a common finding [33]. Moreover, abnormally low erythropoietin levels and blunted erythropoiesis were reported [34]. Management should focus on replacing iron stores and other nutritional deficiencies as necessary. Whether or not the treatment with erythropoietin is beneficial needs further investigation.

Kidney allograft survival does not seem to be affected by pregnancy in recipients with a good graft function [35]. However, those with elevated creatinine levels might have accelerated graft loss. It was shown previously that serum creatinine levels of >1.5 mg/dL and proteinuria of >500 mg/24 h increase the risk of future allograft failure [13,27].

Most recent reports indicate that ≈4.2% of recipients can experience acute rejection during pregnancy [36], therefore careful monitoring of renal function is essential. The incidence of rejection is no higher than in non-pregnant recipients. Adjustment of drug levels due to an increased volume of distribution, as well as weight gain, might be frequently necessary. Also, hyperemesis gravidum can lead to decreased absorption of immunosuppressive medications. Renal blood flow and the GFR can increase by up to 60% during pregnancy, and

therefore any increase in serum creatinine levels should prompt a thorough and timely evaluation, including a kidney transplant biopsy. Davison et al. [27] measured 24-h creatinine clearance before conception and serially in transplant recipients, and compared the values to those from similar studies in healthy women. By the 10th gestational week the mean (SD) 24-h creatinine clearance was 105 (28.1) mL/min (an increase of 34%; range 10–60%), as compared to 124 (15.9) mL/min (an increase of 38%; range 18–69%) in healthy women, with the greatest increase in those whose transplanted kidney functioned best before the conception, regardless of donor source and sex or the transplant-pregnancy interval. In the third trimester the mean (range) 24-h creatinine clearance decreased by 34 (12–57)% in the transplant patients and by 19 (6–28)% in healthy women. The decrease in creatinine clearance in transplant recipients was not associated with the deterioration of allograft function.

Pregnancy outcomes

Perhaps the most comprehensive review of pregnancy outcomes is that of Desphande et al. [36], based on a meta-analysis involving data available from national transplant registries, and from retrospective single-cohort studies published between 2000 and 2010. These authors reported pregnancy outcomes, including miscarriage rates, obstetric complications and delivery outcomes, of 4002 pregnancies in 3570 kidney-transplant recipients, based on the reports from Europe, the Middle East, Asia, North America and Australia. Amongst those, there were 73.5% live births, a 14.0% abortion rate, 2.5% still births and 0.6% ectopic pregnancies. Overall, the rate of live birth was higher than in USA general population (73.4% vs. 66.7%) and varied across the regions, from 69% in Asia to 79% in the Middle East. The incidence of pregnancy-related complications and adverse delivery outcomes were significantly higher in kidney-transplant recipients than in the USA general population (Table 1). The most frequently reported obstetric complication was pre-eclampsia, which was diagnosed in up to a third of recipients, 5–10 times higher than in the non-transplant USA population. However, the diagnosis of pre-eclampsia might not be as reliable as in the non-transplant population due to the higher rates of pre-existing hypertension and proteinuria, potentially undiagnosed before conception. Regardless, the high incidence of pre-eclampsia is of concern, as it carries significant fetal and maternal risks. Moreover, potential risks can extend beyond the pregnancy, as pre-eclampsia has been associated with cardiovascular disease and an increased incidence of ESKD in the long-term follow up after pregnancy [37,38].

Other pregnancy complications, although not as common, were found to be more prevalent than in the general USA population. Gestational diabetes was almost twice as high across all geographical regions, except in Australia (8% vs. 3.9% in transplant recipients and the general population, respectively). The higher incidence of gestational diabetes might be related to the diabetogenic risk of immunosuppressants, including calcineurin inhibitors, corticosteroids and sirolimus. Early and frequent testing with the oral glucose-tolerance test is therefore necessary and might need to be initiated as early as during the first prenatal visit, to unmask unrecognized pre-gestational diabetes [24]. If required, new-onset diabetes should be managed by aggressive dietary modifications and insulin.

Delivery complications are more frequent in this population, with overall 50% of kidney transplant recipients undergoing Caesarean section (vs. 31.9% in the USA general population) and 45% of pre-term deliveries (vs. 12.5% in the general population). The overall gestational age for kidney transplant recipients was 35.8 weeks and the birth weight was 2420 g. Women aged $\leqslant$30 years had more favourable outcomes in terms of live birth and miscarriages [36].

Although registry data and case series indicate a similar incidence of fetal malformation as in the general population, other risks exist, including those related to low birth weight, which can result in various neurological, endocrine, cardiac and renal abnormalities. Moreover, other subtle defects, not apparent at birth, can have life-long consequences, but this requires further evaluation by observational studies [21]. Recommendations for breast feeding remain controversial due to the potential secretion of immunosuppressants in breast milk [39], and additional studies are needed to determine which agents can be safely used during breast feeding. Counselling and thorough discussion about the lack of data on the safety of infant exposure to immunosuppressant agents are important for any mother planning to breast feed [21].

In Middle Eastern countries the incidence of pregnancies is higher than in other regions. Al Duraihimh et al. [41] surveyed transplant centres in Middle Eastern countries and report data from five different countries (Kingdom of Saudi Arabia, Lebanon, Syria, Turkey and Oman). In general, all surveyed centres did not advise against pregnancy, unless the interval from the transplant was <2 years, or there was a history of hypertension or impaired kidney function. The mean prevalence of pregnancy after transplant was 24.1%, with the lowest in Turkey (13%) and the highest in Saudi Arabia (55%). This is in contrast to 12% reported in the UK. The authors speculated that the higher incidence of pregnancies might be related to the social pressure on women to bear a child [41]. Similarly to other regions, pregnant recipients in the Middle East had higher risks of pre-eclampsia (26%), gestational diabetes (7%) and pre-term birth (46%) than in the general population. Caesarean sections were quite common, with an incidence rate of 61%. Rejection rates were as

Table 1 Maternal/fetal complications of pregnancies in kidney transplant recipients.

Group	Complications (%)				
	Miscarriage	Pre-eclampsia	Gestational diabetes	Caesarean section	Pre-term birth
USA general population	17.1	3.8	3.9	31.9	12.5
Overall	14	27	8	56.9	45.6
Asia	12	30	10	51	41
Australia	11	26	1	NR	56
Europe	13	32	7	66	51
Middle East	14	26	7	61	46
North America	15	27	9	44	44
South America	11	21	8	46	46

NR - not reported.

high as 8%, but graft loss after pregnancy was no higher than in other regions [36]. Most importantly, similarly to other countries, recipients with good pre-conceptional kidney function had comparable long-term allograft outcomes to those who were never pregnant.

Living donors

Living-donor kidney transplants are widely accepted and preferable to deceased donor transplants; the possibility of living donations allows an expansion of the donor pool, shortens the time on dialysis, or even avoids the need for dialysis altogether. Superior patient and allograft outcomes after living-donor kidney transplants have been reported often [42]. Living-donor transplantation is predominant, or even exclusive in most Arab countries, due to the strong influence of religion on personal life, and government legislation which requires waiting for procurement and transplantation until religious edicts (fatwas) are passed about the permissibility of organ donation and a diagnosis of brain death [43]. The long-term follow-up of living donors is reassuring, with survival rates and risks of ESKD similar to those in the general population, and an excellent health-related quality of life [44]. Ibrahim et al. [44] followed donors for a mean (SD) of 12.2 (9.2) years after donation, and found that the prevalence of hypertension and albuminuria was similar to controls from the general population matched by age, gender, ethnicity and body mass index. Most importantly, the risk of ESKD was no higher than in the general population.

Most living donors worldwide are women of reproductive age, but the female to male ratio can be reversed in Middle Eastern countries. A recent study from Saudi Arabia showed that men donate more frequently than women (67.4% vs. 32.6%) [45]. This might be due to socio-cultural reasons and overprotection of the female in Middle Eastern societies. However, the authors noted that the rate of female donation in this country is increasing. Although pregnancies in former living donors are considered relatively safe, concerns were raised by reports of a mild increase in blood pressure and proteinuria [46,47].

The most recent contributions to understanding pregnancy outcomes after kidney donation were provided by Reisaeter et al. [48] and Ibrahim et al. [49]. The former study examined data from the Medical Birth Registry of Norway, containing information on the outcomes of pregnancies since 1967. In all, 326 former living donors with 726 pregnancies were identified. Of those, 620 pregnancies occurred before and 106 after the donation. Pregnancies before the kidney donation and a random sample of those not donating kidneys constituted a control group. Ibrahim et al. [49] surveyed 1769 women who donated a kidney at the University of Minnesota; of those, 1085 reported one or more pregnancies, with pregnancies both before and after donation occurring in 98 donors. Table 2 summarises the maternal and fetal complications based on both studies. The outcomes of interest were gestational hypertension, gestational diabetes, pre-eclampsia, low birth weight, prematurity and fetal loss.

Overall, gestational hypertension before and after donation was comparable to that in the general population, based on the Norway birth registry, but it was significantly higher in pregnancies after than before donation in the study of Ibrahim et al. (5.7% vs. 0.6%, respectively; $P < 0.001$). Similarly, a higher risk for gestational diabetes was reported in pregnancies after donation (2.7% vs. 0.7% in the general population; $P < 0.001$). Women who had pregnancies both before and after donation had significantly higher risks for gestational diabetes, hypertension and proteinuria after donation. The rates of pre-eclampsia were lower than in the general population for pregnancies before donation (2.6% based on the Norway Registry, 0.8% at the University of Minnesota, vs. 3.1% in general population), but significantly increased after donation to $>5\%$ in both studies. Women who had babies before and after donation had a significantly increased risk of pre-eclampsia in the latter. Pregnancy after donation was a prominent risk factor for an adverse composite maternal outcome, including gestational hypertension, diabetes and pre-eclampsia. While the adverse maternal outcomes had no future negative effect on kidney function, about half of the women who had gestational

Table 2 Maternal/fetal complications of pregnancies in former living donors.

Complications (%)	General population[a]	Norway		University of Minnesota	
		BD	AD	BD	AD
No. of pregnancies	21,511	6210	106	2723	490
Gestational hypertension	1.5	1.8	2.8	0.6	5.7
Gestational diabetes	NR	NR	NR	0.7	2.7
Preeclampsia	3.1	2.6	5.7	0.8	5.5
Proteinuria	NR	NR	NR	1.1	4.3
Low birth weight	4.8[b]	5.5[b]	7.5[b]	NR	NR
Prematurity	6.6[c]	7.5[c]	9.8[c]	4	7.1
Fetal loss	1.1[d]	1.1[d]	2.8[d]	11.3	19.2

Defined as death, miscarriage and abortion. NR, not reported. BD/AD, before/after donation.

[a] Medical birth registry of Norway.

[b] Defined as <2500 g.

[c] Defined as <37 weeks of gestation.

[d] Stillbirth.

hypertension went onto develop hypertension, and 18% developed proteinuria. Over a third of donors with a history of pre-eclampsia developed proteinuria, and over half became hypertensive [49]. The Norway registry reported similar fetal outcomes to those in the general population. The results of these two studies indicate a slightly higher risk of adverse maternal outcomes in women who decide to become pregnant after donation. However, the current data still leave healthcare professionals with uncertainty about the appropriate counselling of potential donors of child-bearing age. The retrospective nature of published studies and the shortcomings of registry-based and survey-based studies do not provide a definite answer, but rather constitute important background information for future prospective studies. Regardless, the risk of adverse events is small and available data do not support routinely declining potential mothers from donation. Gestational history should also be considered in the donor evaluation, and any woman with a history of gestational complications or pregnancy-induced hypertension should be discouraged from pregnancy after donation, as she could have a higher risk of complications. While there are no guidelines on the timing of pregnancy after donation, waiting 1 year after nephrectomy should be considered, to allow stabilisation of kidney function.

Conclusion

Successful kidney transplantation restores fertility and allows women with ESKD to bear and deliver healthy babies. Although the concerns of safety and pregnancy outcomes are justifiable, with an increased risk of maternal/fetal complications, the risk of negative outcomes is highest in those with suboptimal graft function and multiple comorbidities. Women with stable graft function are much more likely to have successful pregnancies. Counselling before conception, cooperative management with maternal/foetal specialists, and intense antenatal monitoring for complications are all imperative steps to ensure a safe pregnancy. Because the safety and pharmacokinetics of immunosuppressive agents have not been determined, more research is necessary before encouraging their use. Extensive discussion on the potentially higher risks of complications (mainly pre-eclampsia) is a key point when counselling any living donor wishing to conceive after donation. While most women can have successful pregnancies after donation, multicentre prospective studies are crucial to better delineate the risks.

Conflict of interest

No conflict of interest to declare.

References

[1] Lim VS, Henriquez C, Sievertsen G, Frohman LA. Ovarian function in chronic renal failure: evidence suggesting hypothalamic anovulation. *Ann Intern Med* 1980;**93**:21–7.

[2] Kim JH, Chun CJ, Kang CM, Kwak JY. Kidney transplantation and menstrual changes. *Transplant Proc* 1998;**30**:3057–9.

[3] Bagon JA, Vernaeve H, De Muylder X, Lafontaine JJ, Martens J, Van Roost G. Pregnancy and dialysis. *Am J Kidney Dis* 1998;**31**:756–65.

[4] Toma H, Tanabe K, Tokumoto T, Kobayashi C, Yagisawa T. Pregnancy in women receiving renal dialysis or transplantation in Japan: a nationwide survey. *Nephrol Dial Transplant* 1999;**14**:1511–6.

[5] Okundaye I, Abrinko P, Hou S. Registry of pregnancy in dialysis patients. *Am J Kidney Dis* 1998;**31**:766–73.

[6] Hou SH. Frequency and outcome of pregnancy in women on dialysis. *Am J Kidney Dis* 1994;**23**:60–3.

[7] Hladunewich M, Hercz AE, Keunen J, Chan C, Pierratos A. Pregnancy in end stage renal disease. *Semin Dial* 2011;**24**:634–9.

[8] Barua M, Hladunewich M, Keunen J, Pierratos A, McFarlane P, Sood M, et al. Successful pregnancies on nocturnal home hemodialysis. *Clin J Am Soc Nephrol* 2008;**3**:392–6.

[9] Luders C, Castro MC, Titan SM, De Castro I, Elias RM, Abensur H, et al. Obstetric outcome in pregnant women on long-term dialysis: a case series. *Am J Kidney Dis* 2010;**56**:77–85.

[10] Wang GC, Zheng JH, Xu LG, Min ZL, Zhu YH, Qi J, et al. Measurements of serum pituitary-gonadal hormones and investigation of sexual and reproductive functions in kidney transplant recipients. *Int J Nephrol* 2010;**2010**:612126.

[11] Shekhtman MM, Petrova SB. Pregnancy and labor in females with solitary kidney. *Ter Arkh* 2000;**72**:39–42.
[12] Murer L, Zacchello G, Bianchi D, Dall'Amico R, Montini G, Adreetta B, et al. Thrombotic microangiopathy associated with parvovirus B 19 infection after renal transplantation. *J Am Soc Nephrol* 2000;**11**:1132–7.
[13] Yildirim Y, Uslu A. Pregnancy in patients with previous successful renal transplantation. *Int J Gynaecol Obstet* 2005;**90**:198–202.
[14] Keitel E, Bruno RM, Duarte M, Santos AF, Bittar AE, et al. Pregnancy outcome after renal transplantation. *Transplant Proc* 2004;**36**:870–1.
[15] Murray JE. Edith Helm (April 29, 1935-April 4, 2011): the world's longest surviving transplant recipient. *Am J Transplant* 2011;**11**:1545–6.
[16] McKay DB, Josephson MA, Armenti VT, August P, Coscia LA, Davis CL, et al. Reproduction and transplantation: report on the AST consensus conference on reproductive issues and transplantation. *Am J Transplant* 2005;**5**:1592–9.
[17] Armenti VT, Daller JA, Constantinescu S, Silva P, Radomski JS, Moritz MJ, et al. Report from the national transplantation pregnancy registry: outcomes of pregnancy after transplantation. *Clin Transpl* 2006;57–70.
[18] Disease Kidney. Improving global outcomes (KDIGO) transplant work group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant* 2009;**9**(Suppl.):S1–S155.
[19] Umans JG. Medications during pregnancy: antihypertensives and immunosuppressives. *Adv Chronic Kidney Dis* 2007;**14**:191–8.
[20] Merlob P, Stahl B, Klinger G. Tetrad of the possible mycophenolate mofetil embryopathy: a review. *Reprod Toxicol* 2009;**28**:105–8.
[21] McKay DB, Josephson MA. Pregnancy after kidney transplantation. *Clin J Am Soc Nephrol* 2008;**3**(Suppl. 2):S117–25.
[22] Rosenkranz AR, Mayer G. Mechanisms of hypertension after renal transplantation. *Curr Opin Urol* 2000;**10**:81–6.
[23] Kuvacic I, Sprem M, Skrablin S, Kalafatic D, Bubic-Filipi L, Milici D. Pregnancy outcome in renal transplant recipients. *Int J Gynaecol Obstet* 2000;**70**:313–7.
[24] Concepcion BP, Schaefer HM. Caring for the pregnant kidney transplant recipient. *Clin Transplant* 2011;**25**:821–9.
[25] Lindheimer MD, Kanter D. Interpreting abnormal proteinuria in pregnancy: the need for a more pathophysiological approach. *Obstet Gynecol* 2010;**115**:365–75.
[26] Kuo HT, Sampaio MS, Vincenti F, Bunnapradist S. Associations of pretransplant diabetes mellitus, new-onset diabetes after transplant, and acute rejection with transplant outcomes: an analysis of the Organ Procurement and Transplant Network/ United Network for Organ Sharing (OPTN/UNOS) database. *Am J Kidney Dis* 2010;**56**:1127–39.
[27] Davison JM, Milne JE. Pregnancy and renal transplantation. *Br J Urol* 1997;**80**(Suppl. 1):29–32.
[28] Levine D, Filly RA, Graber M. The sonographic appearance of renal transplants during pregnancy. *J Ultrasound Med* 1995;**14**:295–6.
[29] Thompson BC, Kingdon EJ, Tuck SM, Fernando ON, Sweny P. Pregnancy in renal transplant recipients: the Royal Free Hospital experience. *QJM* 2003;**96**:837–44.
[30] Thomas AA, Thomas AZ, Campbell SC, Palmer JS. Urologic emergencies in pregnancy. *Urology* 2010;**76**:453–60.
[31] Arthurs SK, Eid AJ, Pedersen RA, Kremers WK, Cosio FG, Patel R, et al. Delayed-onset primary cytomegalovirus disease and the risk of allograft failure and mortality after kidney transplantation. *Clin Infect Dis* 2008;**46**:840–6.
[32] Hou S. Pregnancy in renal transplant recipients. *Adv Ren Replace Ther* 2003;**10**:40–7.
[33] Barroso F, Allard S, Kahan BC, Connolly C, Smethurst H, Choo L, et al. Prevalence of maternal anaemia and its predictors: a multi-centre study. *Eur J Obstet Gynecol Reprod Biol* 2011;**159**:99–105.
[34] Magee LA, von Dadelszen P, Darley J, Beguin Y. Erythropoiesis and renal transplant pregnancy. *Clin Transplant* 2000;**14**:127–35.
[35] Gutierrez MJ, Gonzalez P, Delgado I, Gutierrez E, Gonzalez E, Siqueira RC, et al. Renal allograft function and cardiovascular risk in recipients of kidney transplantation after successful pregnancy. *Transplant Proc* 2009;**41**:2399–402.
[36] Deshpande NA, James NT, Kucirka LM, Boyarsky BJ, Garonzik-Wang JM, Montgomery RA, et al. Pregnancy outcomes in kidney transplant recipients: a systematic review and meta-analysis. *Am J Transplant* 2011;**11**:2388–404.
[37] Bellamy L, Casas JP, Hingorani AD, Williams DJ. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *BMJ* 2007;**335**:974.
[38] Vikse BE, Irgens LM, Leivestad T, Skjaerven R, Iversen BM. Preeclampsia and the risk of end-stage renal disease. *N Engl J Med* 2008;**359**:800–9.
[39] American Academy of Pediatrics Committee on Drugs. The transfer of drugs and other chemicals into human milk. *Pediatrics* 1994;**93**:137–50.
[41] Al Duraihimh H, Ghamdi G, Moussa D, Shaheen F, Mohsen N, Sharma U, et al. Outcome of 234 pregnancies in 140 renal transplant recipients from five middle eastern countries. *Transplantation* 2008;**85**:840–3.
[42] Matas AJ, Gillingham KJ, Humar A, Kandaswamy R, Sutherland DE, Payne WD, et al. 2202 Kidney transplant recipients with 10 years of graft function: what happens next? *Am J Transplant* 2008;**8**:2410–9.
[43] Al Sayyari AA. The history of renal transplantation in the Arab world: a view from Saudi Arabia. *Am J Kidney Dis* 2008;**51**:1033–46.
[44] Ibrahim HN, Foley R, Tan L, Rogers T, Bailey RF, Guo H, et al. Long-term consequences of kidney donation. *N Engl J Med* 2009;**360**:459–69.
[45] Guella A, Mohamed E. Donor and recipient gender distribution in a Saudi kidney transplant center. *Transplant Proc* 2011;**43**:415–7.
[46] Boudville N, Prasad GV, Knoll G, Muirhead N, Thiessen-Philbrook H, Yang RC, et al. Meta-analysis: risk for hypertension in living kidney donors. *Ann Intern Med* 2006;**145**:185–96.
[47] Garg AX, Muirhead N, Knoll G, Yang RC, Prasad GV, Thiessen-Philbrook H, et al. Proteinuria and reduced kidney function in living kidney donors: a systematic review, meta-analysis, and meta-regression. *Kidney Int* 2006;**70**:1801–10.
[48] Reisaeter AV, Roislien J, Henriksen T, Irgens LM, Hartmann A. Pregnancy and birth after kidney donation: the Norwegian experience. *Am J Transplant* 2009;**9**:820–4.
[49] Ibrahim HN, Akkina SK, Leister E, Gillingham K, Cordner G, Guo H, et al. Pregnancy outcomes after kidney donation. *Am J Transplant* 2009;**9**:825–34.