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POSITION PAPER AND GUIDELINE

Best practices on pregnancy on dialysis: the Italian Study Group on Kidney and Pregnancy

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Abstract
Background Pregnancy during dialysis is increasingly being reported and represents a debated point in Nephrology. The small number of cases available in the literature makes evidence-based counselling difficult, also given the cultural sensitivity of this issue. Hence, the need for position statements to highlight the state of the art and propose the unresolved issues for general discussion.
Methods A systematic analysis of the literature (MESH, Emtree and free terms on pregnancy and dialysis) was conducted and expert opinions examined (Study Group on Kidney and Pregnancy; experts involved in the management of pregnancy in dialysis in Italy 2000–2013). Questions regarded: timing of dialysis start in pregnancy; mode of treatment, i.e. peritoneal dialysis (PD) versus haemodialysis (HD); treatment schedules (for both modes); obstetric surveillance; main support therapies (anaemia, calcium-phosphate parathormone; acidosis); counselling tips.
Main results Timing of dialysis start is not clear, considering also the different support therapies; successful pregnancy is possible in both PD and HD; high efficiency and strict integration with residual kidney function are pivotal in both treatments, the blood urea nitrogen test being perhaps a useful marker in this context. To date, long-hour HD has provided the best results. Strict, personalized obstetric surveillance is warranted; therapies should be aimed at avoiding vitamin B_{12}, folate and iron deficits, and at correcting anaemia; vitamin D and calcium administration is safe and recommended. Women on dialysis should be advised that pregnancy is possible, albeit rare, with both types of dialysis treatment, and that a success rate of over 75 % may be achieved. High dialysis efficiency and frequent controls are needed to optimize outcomes.

Keywords Chronic kidney disease · Hemodialysis · Peritoneal dialysis · Dialysis efficiency · Evidence based medicine · Daily dialysis

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Introduction

From the first reports in the early 1970s of successful pregnancy in dialysis up until the year 2000, pregnancy during dialysis was considered an exceptional occurrence, alternatively considered a miracle or an event to be discouraged due to both the maternal and the foetal risks [1–

4]. The scenario in the new millennium has changed somewhat for at least three main reasons.

Firstly, the diffusion of dialysis in countries where attitudes towards pregnancy and chronic diseases differ from western countries and where a strong cultural drive towards large families and less influence of "invisible" diseases such as end-stage renal disease (ESRD) on social life may be observed has made it possible to collect large series of dialysis patients undergoing successful pregnancies, thus leading to a more positive approach to pregnancy in dialysis [5–10]. Secondly, the impressive increase in dialysis efficiency provided by "intensive" non-conventional schedules (mainly long-hour nightly dialysis) has allowed us to achieve unprecedented results in pregnant women on dialysis, confronting the nephrological community with the need for a new standard of dialysis efficiency [11–13]. Thirdly, the growing trend towards empowering patients is changing the attitude regarding decisions that were once "contraindicated", and may be one of the reasons for the increase in pregnancy in women on dialysis in the western world [14, 15].

The Italian Study Group on Kidney and Pregnancy has undertaken a nationwide survey on pregnancy in chronic dialysis and transplantation, allowing us to quantify the Italian experience in the new millennium [16]. The odds of having a child on dialysis are about 1:100 with respect to the Italian population of the same age group, and about 1:10 with respect to grafted women. These data are in agreement with results of the ANZDATA Registry which reported the results of a large survey carried out in Australia and New Zealand [17, 18]. Our study on pregnancy in on-dialysis women in Italy was an opportunity to increase awareness on this topic in our country and to set the stage for the present "best practice" review.

Evidence-based medicine and pregnancy in dialysis: methodological insights

The evidence concerning pregnancy during dialysis is subject to certain methodological issues related to pregnancy per se and to rare events. The first issue regards randomized trials. Clearly, pregnancy itself cannot be randomized and, furthermore, randomization of any treatment in pregnancy is complex, and often ethically unfeasible. Therefore, no randomized controlled trials (RCTs) are foreseen to study dialysis duration, frequency or schedules in association with pregnancy or obstetric care policies.

The second issue is that rare occurrences are more subject to publication and reporting biases: the happy ending of a rare event prompts communication, while the opposite is true in cases of catastrophic events, such as the loss of the mother and/or child. Hence, the evidence is heterogeneous and scant, with several case reports showing referral and publication biases, and few existing large series from reference Centres or Registries. Currently, despite growing interest in this topic, only the ANZDATA dialysis Registry gathers data on pregnancies in its core file, while the US Registry on Pregnancy and Dialysis is based upon voluntary contribution and the ERA-EDTA has only recently commenced a specific study on this issue, i.e. the DIAPER study [11, 17–19].

Therefore, while acknowledging the lack of RCTs (by necessity of the subject, i.e. pregnancy) and of large observational studies (due to the rarity of the event), we will here deal at best with GRADE IIa recommendations, though we also need to consider several non graded suggestions (which should not be underestimated) that may be seen as reflecting an ever-evolving situation [20–25].

The present position statement refers to a search strategy that was based on the June 2014 update of a previous systematic review on dialysis and pregnancy. Details on the search strategy and on the paper selection modality can be found in that review [5].

"Diagnosis" of pregnancy in dialysis

1. The "diagnosis" of pregnancy in women on dialysis may be difficult, and the presence of the foetus and the gestational age should be verified by ultrasound examination (not graded).

The "diagnosis" of pregnancy in the dialysis setting may be difficult both because pregnancy is often unexpected and the symptoms in the early phase may mimic different diseases and complications of dialysis, and because serum levels of beta-hCG may be increased even in the absence of pregnancy [26, 27]. Furthermore, irregular menstrual cycles and anovulation are common in women on dialysis, thus making the calculation of gestational age based upon the last menstrual cycle unreliable [26]. In this context, early ultrasonography should be used to verify the presence of a viable foetus and to calculate the gestational age.

Timing of start of dialysis in pregnancy

1. Initiate renal replacement therapy (RRT) when a good metabolic and fluid balance cannot be achieved by conservative treatment (not graded).
2. When deciding to start RRT, take into consideration the general clinical context including the presence of conditions that can be modified by dialysis, the trend of the subject's laboratory tests, and control of

hypertension and fluid overload rather than creatinine-based thresholds alone (not graded).
3. Consider urea levels in the decision when to start dialysis: the blood urea nitrogen (BUN) test is considered a very important marker of outcomes when dialysis is already started. No threshold has been established for dialysis start (not graded).
4. Consider the phase of pregnancy in the decision, balancing the risks and benefits of dialysis start versus early delivery in late pregnancy (after the 28th and, more specifically, after the 34th gestational week) (not graded).
5. Low protein diets may be useful for postponing dialysis in selected cases with advanced chronic kidney disease (CKD) (not graded).

'Life-threatening' changes in fluid, electrolyte and acid–base balance that cannot be managed by conservative interventions are the main indications for dialysis start [28, 29]. The concept of "life-threatening" is, however, difficult to apply to pregnancy and no studies have specifically focused on this issue. One of the problems also is the limited reliability of estimated glomerular filtration rate (eGFR) assessment in pregnancy due to the lack of validated formulae [28–32].

The cases reported in the literature range from "early" dialysis start, at a GFR of about 20 ml/min, to a later start, in keeping with the most recent guidelines [18, 33, 34].

All the available data on dialysis start come from observational studies focusing on various outcomes. However, the impressive relationship between pregnancy-related outcomes and dialysis efficiency suggests that once dialysis is started treatment should be intensive [11–13].

The main benefits of RRT on metabolic control and on volume and blood pressure management versus the potentially negative effects on the mother and foetus should be weighed up on an individual basis. These drawbacks include catheter-related complications if dialysis is started with a central venous access, the need for surgical intervention and the stress related to fistula placement, haemorrhaging caused by anticoagulation therapy, and the risk of dialysis-related hypotension that may precipitate foetal–placental hypoperfusion, a feared side-effect of diuretics [33–35].

The risk–benefit balance may be different in the various phases of pregnancy, and the balance may be in favour of start of dialysis in early pregnancy, while the risks of dialysis should be carefully weighed against the risks of early delivery. This is especially true after the 34th completed gestational week, on account of the important reduction of major foetal risks after this term (the "late preterm period" is defined as 34–37 gestational weeks) [36–39]. Every effort should be made to prolong pregnancy as much as possible in the "grey" area in which viability is possible but the risk of long-term problems is very high ("extremely preterm period": 24–28 weeks) [38, 39].

According to the decade-long experience of a single nephrology and obstetrics group in managing severe CKD, a low-protein diet under strict clinical control may be useful for postponing dialysis in selected cases [40, 41].

These mostly experience-based opinions underline the need for further studies on the timing of dialysis start in pregnancy. Hence, the Study Group on Kidney and Pregnancy of the Italian Society of Nephrology encourages systematically including detailed indications for the start of dialysis (also with regard to the foetal situation) in reports on dialysis in pregnancy, and identifying control groups treated conservatively or with planned delivery before dialysis start.

Haemodialysis or peritoneal dialysis in pregnancy?

1. In patients already on dialysis when the pregnancy starts, dialysis can be continued in the same mode provided that a good dialysis efficiency is reached (evidence from scattered reports).
2. For patients who need to start dialysis when a pregnancy is underway, the following issues should be taken into consideration: the patient's preference, phase of pregnancy, expected dialysis efficiency, availability of intensive extracorporeal dialysis and risk of rapid loss of kidney function (not graded).

There are currently no studies specifically comparing peritoneal dialysis (PD) and extracorporeal dialysis (HD) in pregnancy, though some reports of pregnancies in association with both dialysis modalities are available in many large series or from registry data [5, 16–18, 42, 43].

The smaller number of cases reported for PD is at least partly a reflection of the overall lower prevalence of this technique. However, in the light of data on extracorporeal dialysis suggesting a close link between favourable outcomes and dialysis efficiency, the possibility of a negative effect of the lower dialysis efficiency should be taken into account.

The Study Group recommends taking the following issues into consideration when choosing the type of dialysis. The patient's preference should be the main criteria for the choice, provided there are no contraindications for either method. The phase of pregnancy may be relevant, in particular in the late phases of pregnancy and even more so in specific diseases such as autosomal dominant polycystic kidney disease (ADPKD) in which abdominal filling may be critical and the risk of uterine injury may be increased due to mechanical reasons. Furthermore, with regard to dialysis start, due to the acknowledged importance of this

issue, the Italian Study Group suggests to consider the expected dialysis efficiency and the availability of intensive extracorporeal dialysis. To date, the best results published regarding pregnancy in RRT were obtained with long-hour daily dialysis; therefore we suggest considering this as first choice, when available, although there is no evidence suggesting that "less intensive" extracorporeal schedules and intensive PD may lead to different pregnancy-related outcomes [11, 12]. A further issue may be the risk of rapid loss of residual renal function, which is expected to be higher with HD than with PD. This point in favour of PD should be evaluated also bearing in mind the previous decline of residual renal function, as this is expected to be more relevant in chronic interstitial diseases in which, outside of pregnancy, the loss of kidney function is usually slower than in primary or secondary glomerular diseases [44, 45].

Conversely, the disadvantages of each of the two therapies, namely, the risk of peritonitis and lower efficiency of PD, on the one hand, and the risk of overly rapid fluid and electrolyte shifts, of anticoagulation and the higher intrusiveness in one's daily life of HD, on the other, should be mentioned in counselling.

There is a strong need for prospective observational comparative studies on this issue. The Italian Study Group suggests adding data regarding pregnancy to the yearly update of dialysis registries.

Dialysis schedule for haemodialysis

1. Haemodialysis is the standard extracorporeal treatment in pregnancy; few data are available regarding haemodiafiltration, thus suggesting at least equal benefits (not graded).
2. Haemodialysis intensity (frequency and duration) should be increased in pregnancy (strong recommendation, good quality observational evidence).
3. Quotidian or nightly dialysis (6–7 days per week) should be offered at least to patients without residual renal clearance (strong recommendation, good quality observational evidence).
4. Since pregnancy outcome improves as the number of dialysis hours increases, reaching statistical significance at or above 36 h per week (85 % probability of success), we suggest tailoring the number of hours needed to reach this minimum goal as quickly as possible (strong recommendation, good quality observational evidence).
5. We recommend adapting the prescription of bicarbonate, potassium and calcium to the individual patient, with particular attention to slow fluid removal and to the progressive increase in weight during pregnancy (not graded).
6. We do not recommend using Kt/V or equivalent renal clearance as a measure of dialysis in pregnancy due to the lack of studies evaluating these markers; pre-dialysis BUN levels (<50 mg/dl) or urea levels (<100 mg/dl) may be used as a surrogate (not graded).

Due to the rarity of pregnancy during dialysis, to the scattered data and to the varying availability of dialysis all over the world, there is a considerable lack of data on extracorporeal dialysis other than bicarbonate dialysis, even though from a theoretical point of view haemodiafiltration may be more suited to pregnancy given the high tolerance and better removal of middle molecules afforded by this method. There are few reports in the literature regarding this dialysis modality, overall suggesting that haemodiafiltration may be (at least) equal to haemodialysis in pregnancy [46–49].

Long, highly efficient daily haemodialysis treatments have been increasingly used in pregnancy. The best results on dialysis, at least in cases without residual kidney function, have been reported in long-hour daily dialysis [5, 11–13, 18, 46–56].

The use of Kt/V or urea levels for tailoring dialysis is not recommended since none of these measurements has been validated in pregnancy and their role as markers of "optimal efficiency" is clearly not applicable to pregnancy, a situation in which available data suggest a policy of "the more the better" [5, 11–13, 46–56]. A pre-dialysis urea level below 100 mg/dl may be considered a useful surrogate marker on the basis of the Canadian experience with long-hour daily dialysis [11–13].

Normal pregnancy is a hyperdynamic hyperhydrated state; this should be kept in mind when tailoring weight loss on dialysis. The usual markers of hydration in dialysis, i.e. blood pressure or muscle cramps, may be altered in pregnancy, the former by physiological vasodilation, the latter by the frequent occurrence of cramps in pregnancy, even in the absence of evident electrolyte disorders. None of the other means of establishing the "dry weight", including bioimpedance or brain natriuretic peptide levels, has been validated in pregnancy. Hence, we suggest tailoring the decision on the type of dialysis to the individual patient, taking into account the usual tools available for assessment in each Unit and the specific experience of the clinicians.

Once more, the Study Group encourages systematically including detailed information of the dialysis schedules in all future studies to allow better contextualization of the results.

Dialysis schedule for peritoneal dialysis

1. What the "ideal" type of peritoneal dialysis is—continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD)—remains to be determined (not graded).
2. Dialysis efficiency has to be increased to provide increased solute clearance in women on PD who are pregnant (not graded).
3. In CAPD, the peritoneal dialysis prescription should be modified by increasing the *number* of exchanges rather than the exchange volume since large volumes are not well tolerated, especially during the third trimester (not graded).
4. In APD, the dialysis prescription should be modified with an increase in the total volume and prolonged time, reducing dwell volumes and increasing the number of cycles (not graded).
5. In APD, tidal peritoneal dialysis can be used to avoid drain pain and reduce gastro-oesophageal reflux. Tidal regimens may also alleviate catheter drain dysfunction caused by the expanding uterus (not graded).
6. We do not recommend using Kt/V and/or peritoneal creatinine clearance as a measurement of dose of dialysis in pregnancy due to the lack of studies considering these markers with respect to pregnancy outcomes (not graded).

There are fewer studies on PD as compared to HD: conception rate is reported as being lower in PD patients, even though the reported ranges are broad, as was also recently confirmed by the ANZDATA Registry [3, 4, 17, 40, 57–68]. This lower conception rate has been attributed to several factors, including the presence of hypertonic dialysate in the peritoneum, prior episodes of peritonitis and the inability of the ovum to reach the fallopian tubes in the presence of intraperitoneal dialysate [44, 69].

Dialysis prescriptions should be tailored to increase peritoneal clearance, mainly by acting on the frequency and/or duration of dwell, avoiding an increase in volumes, and taking abdominal fullness into account [3, 4, 17, 44, 57–69].

Several advantages and disadvantages of PD have been reported: some authors have suggested that the main disadvantages include: abdominal fullness with the possibility of catheter displacement, drain pain, dialysate flow disturbance and gastro-oesophageal reflux. Haemoperitoneum is an infrequent and usually benign occurrence in patients treated with peritoneal dialysis that is occasionally reported in pregnancy. Management strategies include increased exchanges and cooled dialysate. Severe haemoperitoneum that does not clear may be a sign of uterine trauma, uteroplacental detachment, placenta previa, or spontaneous abortion [60, 67–70]. The incidence of peritonitis is not reported as being higher than what is observed in patients who are not pregnant [67–70].

Conversely, peritoneal dialysis offers some advantages: continuous treatment with smoother urea removal and stable metabolic balance without the fluctuations that are typical of the intermittent therapies; gentle daily ultrafiltration, minimizing changes in maternal intravascular volumes without the acute fluctuations that can compromise placental blood flow. Other potential benefits may be had by avoiding systemic anticoagulation, and possibly by following a more liberal diet, at least with regard to the many potassium rich foods.

When caesarean section is required, and if it is performed extraperitoneally, peritoneal dialysis can be resumed with small dwell volumes after 24 h, otherwise the mother should be temporarily switched to haemodialysis [71].

Diet and weight management

1. The patient's diet should be unrestricted and rich in proteins (supported by several experts; not graded).
2. Phosphate supplements may be needed on long-hour daily haemodialysis (not graded).
3. Soluble vitamin levels should be controlled and supplemented when needed (not graded).
4. Weight gain should be carefully monitored, trying to avoid dehydration and hypotension. Weight gain is estimated at 300 g/week during the second trimester and 300–500 g/week in the third trimester (not graded).

Nutritional support is mentioned in several papers, and overall the most common advice is either an unrestricted diet or a high protein diet [3, 11–13, 49, 50, 53, 72–74]. Nutritional supplements of phosphate may be needed in patients treated with high efficiency, long-hour dialysis, while water-soluble vitamins should always be checked in all patients and supplemented when needed. While daily, high efficiency dialysis is increasingly being prescribed, it usually suffices to correct acidosis and restore a positive calcium balance, although other trace elements, including zinc, may be deficient and should be kept under control and supplemented if necessary [11–13, 75].

The limits of these indications are linked to the fact that different nutrients are reported across the various studies, and that there is no shared list of vitamins and microelements that should be controlled. In the absence of precise indications, the Italian Study Group suggests including detailed testing and supplementation policies in studies on pregnant women on dialysis.

Control policies

1. We recommend strict clinical control for all patients (not graded).
2. The frequency of visits should be personalized; weekly laboratory controls are recommended to tailor dialysis schedules (not graded).
3. We do not suggest pre-emptive hospitalization except for obstetrics-related reasons (not graded).
4. Obstetric and nephrological visits should be combined to minimize stress on the patient (not graded).
5. Foetal monitoring should be intensified (supported by all experts; not graded).

Again, there is no specific evidence available on this very important clinical issue. Very few papers report the frequency of visits in detail and, in the few papers that do report on them, the non homogeneity of policies for the management of chronic dialysis patients is evident [3–13, 16–18, 43, 44, 50–53].

In this context, the opinion of the Italian Study Group is that intensifying dialysis requires concomitantly intensifying clinical and biochemical testing. The tests, which are usually linked to the dialysis session (creatinine, urea, electrolytes, complete blood cell count, acid base balance, serum albumin), should be performed at least twice monthly in stable patients. However, the frequency may be further increased in specific patients and in Centres having less experience with quotidian dialysis treatments.

The reported obstetrics control policy is highly heterogeneous, following the general changes that have taken place in obstetrics policies over time. Older papers underline the importance of uterine and foetal monitoring at each dialysis session [53–56, 69–73]. Conversely, more recent studies report less stringent controls, such as ultrasounds every 1–2 weeks or more frequently as the patient nears term, or when pregnancy complications are encountered. Some authors also suggest including serial cervical length measurements [6, 7, 11, 54]. Recent studies underline the importance of Doppler measurements every 1–3 weeks [6, 7, 11, 55, 56]. In such context, even taking into account the different policies in the various obstetric referral centres, our Study Group suggests contextualizing the control policy with the obstetricians.

Main drug treatments: anaemia

1. Anaemia should be managed with erythropoietin stimulating agents (ESAs) and vitamins. The haemoglobin target should be 10–11 g/dl. ESA doses frequently need to be increased in pregnant dialysis patients (strong suggestion from large studies on CKD patients not on dialysis).
2. The demand for iron is increased in pregnancy in dialysis. Oral iron administration is safe in pregnant women on dialysis, while intravenous (i.v.) iron should be managed with care in dialysis mothers (strong suggestion from large studies in CKD patients not on dialysis and in non CKD patients).
3. Folate and B_{12} supplementation should be tailored according to blood levels (not graded).

Anaemia is a frequent complication in pregnant dialysis patients [3–5]. However, most of the information from the large series regards patients not on dialysis. Maternal anaemia has been correlated with infant mortality, preterm labour and foetal loss in large series of non-dialysis patients [76–81]. Erythropoietin has been shown to be safe and non-teratogenic in pregnancy [79–81]. Erythropoietin doses should be increased by 50–100 % in an attempt to achieve targeted haemoglobin levels above 10–11 g/dl, with haematocrit concentrations above 30–35 % [5, 13, 27].

The need for iron, which is already an issue in healthy pregnant women, may be higher in pregnant women on dialysis [69]. Oral iron administration is safe in pregnancy, although it is often not sufficient to compensate for the increased need: supplementation should start as soon as possible in the presence of even only a mild deficiency and normal haemoglobin levels [82–86]. In refractory cases, intravenous iron, targeted at transferrin saturation levels above 30 %, has been given to pregnant dialysis patients without adverse events [13, 82–86]. However, in the later stages of pregnancy, up to 80–90 % of parenteral iron may be deposited in the foetus; thus it should be given in small doses [69]. Folate and B_{12} should be checked and supplemented in the case of low blood levels at doses adjusted to reach appropriate levels in the blood [69].

Main drug treatments: calcium-phosphate balance

1. Vitamin D supplementation is safe in pregnancy and may be required at increased doses (strong suggestion from large studies in non-dialysis patients).
2. Calcium-containing phosphate binders are safe (not graded), while sevelamer may negatively affect foetal ossification (evidence from animal studies).
3. Attention should also be paid to magnesium levels since low levels may favour uterine contraction (strong suggestion from large studies in non-dialysis patients).

The need for vitamin D supplementation is increasingly acknowledged in pregnancy [87–90]. In pregnant dialysis patients the usual vitamin D needs may be increased

because of placental 25-hydroxyvitamin D3 conversion [91]. In dialysis patients, vitamin D supplementation should be guided by levels of mono and di-hydroxylated vitamin D, calcium and phosphate [92]. Calcium supplements or calcium-based binders are safe, but their use may not be needed if high dialysis efficiency is attained, while sevelamer should not be used in pregnancy because animal studies have shown irregular ossification of foetal bones [91, 92].

Magnesium is a tocolytic and low serum levels may induce uterine contractions. Serum magnesium levels should be maintained at 5–7 mg/dl; oral magnesium supplementation may be required [91, 93].

Other drug treatments, such as hypotensives or aspirin, will be discussed in the next consensus statement on CKD and pregnancy.

Counselling tips for dialysis or pre-dialysis patients who wish to undertake a pregnancy

1. Counselling on pregnancy and contraception should be included in the approach to all women in childbearing age who start dialysis (not graded).
2. Extensive counselling is needed to guide the choice of a woman on dialysis whether to undertake or continue pregnancy (not graded).
3. The prognostic markers allowing quantification of the probability of a successful pregnancy are only partially known. Residual kidney function and normotension are favourable prognostic factors (not graded).
4. Counselling should also include the fact that outcomes of pregnancy are better after transplantation than on dialysis (strong suggestion from large studies in transplanted patients, and from Registries).
5. The main risks for the child are those linked to prematurity. No increase in congenital malformations has been reported (not graded).

Counselling is a crucial part of the care of a pregnant woman on dialysis and should be systematically undertaken before pregnancy and possibly also before the start of dialysis [5, 74, 94]. Counselling on pregnancy is closely linked to counselling on contraception, as the effect of an unwanted pregnancy may be disruptive on a woman on dialysis. With regard to the indications for clinical counselling, it should be extensive and should cover the most important evidence, as well as the limits of the current knowledge and experience. According to the Study Group, the following issues should be covered: pregnancy on dialysis is possible and the reported success rate has been over 70–80 % in the last decade [5–13]. However, evidence is scant, and there is probably a bias of reporting only the "happy endings", at least in smaller case series. The risk of death for the mother is very low with no deaths being reported in the most recent large series [5–13]. The risk of foetal loss and of neonatal death is higher than in pregnancy after transplantation and is higher in both cases with respect to the overall population [16, 17].

Prematurity is the main risk for the baby. Besides the presence of hereditary kidney diseases, there is no evidence suggesting that the number of congenital malformations is higher in children born to dialysis mothers. The risk of prematurity is, however, very high and decreases along with the increase of dialysis frequency and time on dialysis [5–13, 16, 17, 42, 95]. In the very few studies reporting long-term outcomes in children, normal psychosocial skills have been reported in most cases [16, 44]. Considering the importance of this subject, the Italian Study Group strongly suggests the need for further studies on the long-term prognosis of mothers and children.

Dialysis care in pregnancy is highly demanding: there is a need to increase the number and duration of haemodialysis sessions, with an ideal target of at least 36 h per week. Even if there is no need a priori to change the dialysis modality if the mother is on PD, (but even in this case) efficiency should be increased as much as possible, and a shift to haemodialysis may be needed if metabolic control is suboptimal [5–13, 16, 17, 49–52].

The presence of residual renal function is reported as being correlated to better pregnancy related outcomes, as is a shorter dialysis vintage and the starting of dialysis during the course of pregnancy (as opposed to conception occurring when dialysis is underway) [16–18]. However, pregnancy is also possible in patients with long-term dialysis vintage, no residual kidney function and immunological diseases [16, 18].

In spite of the growing number of cases reported in the literature, the Working Group underlines that patients should be made aware that clinical experience is still limited and that even the largest eferral Centres have dealt with a very limited number of cases.

Patients should also be advised that the probability of a successful at, or near, term pregnancy is significantly higher in patients after transplantation than in patients on dialysis. This may support the choice of postponing pregnancy until after kidney transplantation, at least in patients who are young and have a high probability of receiving a kidney graft [16, 17, 96–98].

Despite all these limits, dialysis patients may benefit from all the advantages that have been reported in maternal-foetal medicine in the last decades, and the outcomes of pregnancy on dialysis have improved in all studied settings in the new millennium due to well-established cooperation between the Nephrology team and tertiary Obstetrics care Centre.

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Conflict of interest The authors declare they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Appendix: Working Group on Dialysis and Pregnancy

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