Renal and Bladder Cancer During Pregnancy: A Review of 47 Cases and Literature-based Recommendations for Management

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Manuscript

Introduction

The incidence of renal and bladder cancer in the general population is respectively 5.3 and 7.2 per 100.000.¹ Urological malignancies have a lower prevalence during the reproductive years, with a peak incidence, predominantly in males, occurring between 60 and 70 years of age. Obesity, smoking and hypertension are well-established risk factors for renal cell carcinoma. Bladder cancer is associated with exposure to cigarette smoking and chemicals (e.g. nitrosamine).² Screening for underlying hereditary cancer syndromes such as Lynch syndrome and Von Hippel-Lindau disease may be considered due to the young age at presentation. Urological cancer during pregnancy is extremely rare, affecting approximately 13 of 1.000.000 pregnancies.³ Signs of urological cancer such as hematuria, urgency, hypertension and low back pain may be attributed to pregnancy. In addition, the reluctance of performing imaging during pregnancy can lead to a delayed diagnosis.

Both the outcome for the pregnant patient and the unborn child must be taken into account in clinical decision-making, which is challenging and requires a multidisciplinary approach. The aim of this study is to give an overview of the obstetric and maternal outcomes of patients with a diagnosis of renal or bladder cancer during pregnancy and to provide gestational age-specific recommendations for management.

Materials and Methods

The International Network on Cancer, Infertility and Pregnancy (INCIP) (www.cancerinpregnancy.org), supported by the European Society of Gynecologic Oncology (ESGO), launched a registry of pregnant patients diagnosed with cancer. The study was approved by the ethical committee of the university hospitals of Leuven,

Belgium and registered on ClinicalTrials.gov, number NCT00330447. Oncological and obstetric data of all patients diagnosed with primary or recurrent renal or bladder cancer during pregnancy were retrieved from the INCIP database. Patients diagnosed with cancer postpartum were excluded. Birth weight percentiles were determined using the customized calculator derived from www.gestation.net, adjusting for ethnicity, parity, height and weight of the mother, and gender of the neonate. Small for Gestational Age (SGA) was defined as a customized birth weight below the 10th percentile.

Retrieved INCIP cases were diagnosed between 1999 and 2017. In order to give an overview of most recent cases in the English literature from the same time period, a review of literature was performed using PUBMED. Articles were identified using the MESH terms 'Urological Neoplasms', 'Pregnancy', 'Renal Neoplasms' and 'Urinary Bladder Neoplasms', and variations hereof. For renal cases, case reports published since the latest review from 2014 were collected.⁴ A recent Belgian case series of six pregnancy-associated renal malignancies was not included as reported cases were also included in the INCIP registry.⁵ For bladder cancer all new cases published after the last large series (27 cases) in 2004 were reviewed.⁶ Only descriptive statistics were performed. Obstetric outcome was reported for all cases, regardless of pregnancy outcome. The neonatal outcome of the INCIP cases was presented in detail.

Results

From the INCIP registry, 22 patients diagnosed with renal (n=14) or bladder cancer (n=8) during pregnancy were retrieved (Supplementary Table 3 and 4). Patients were registered in eight different countries (Belgium, Italy, USA, Greece, Czech Republic, Mexico, Germany and the Netherlands). In the literature, 15 and 10 cases of renal and bladder cancer respectively, were reported since last large case series

(Supplementary Table 5 and 6).⁷⁻²⁸ Most symptomatic patients presented with loin pain (renal cancer) or hematuria (bladder cancer) (Table 1 and 2). In 16 patients (16 of 47, 34%) the tumor was detected while performing routine prenatal ultrasound.

Oncological data

The management of renal and bladder cancer according to gestational age at diagnosis is presented in Figure 1.

For 29 patients with renal cancer, the most common histological type of cancer diagnosed was clear cell type carcinoma (13, 45%) and the majority of patients presented with tumors limited to the kidney (stage I or II) (Table 1). Gestational age at elective surgery in 17 patients (59%) varied between 7 weeks and 29 weeks.

For 18 patients with bladder cancer, the most common subtype was urothelial cell carcinoma (UCC; 13, 72%) and half of patients (9,) had disease that did not infiltrate into the connective tissue or muscular layer of the bladder (TaN0M0) (Table 2). Surgical resection was performed between 10 and 39 weeks of gestation in 10 patients (56%); all were diagnostic trans-urethral resection of bladder tumor (TURBT) except one patient with an exploratory laparotomy with partial bladder resection of an urachal duct squamous cell carcinoma in early pregnancy.²⁰

Obstetric outcome

Because of renal cancer diagnosis, two pregnancies were terminated in the first half of pregnancy. Another patient spontaneously miscarried after a nephrectomy for stage II renal cell carcinoma (RCC) at 7 weeks of gestation. Two patients diagnosed with renal cancer, had a stillbirth; One intra-uterine fetal demise occurred at 24 weeks of gestation, 1 month following laparotomy for renal cancer. Another patient presented with hemorrhagic shock secondary to spontaneous rupture of a renal tumor at term.¹⁷ An emergency laparotomy could not prevent maternal and fetal death. The other 21

pregnancies (80%) with a reported obstetric outcome ended in a livebirth, including one twin pregnancy (Table 1). Ten out of 11 patients (91%) that delivered after 37 weeks underwent surgery during pregnancy. Eight of 10 patients (80%) delivered preterm for oncological reasons.

For bladder cancer, there was one early pregnancy terminated for stage IV cancer. The 16 pregnancies (94%) with reported obstetric outcome ended in livebirths, including two twin pregnancies (Table 2). In 7 of 9 patients (78%) that delivered term prenatal surgery was performed. Four of 7 patients (57%) who delivered prior to 37 weeks had an elective delivery in order to initiate surgical or systemic treatment.

Neonatal outcome of INCIP cases

In the INCIP study population 17 singletons (excluding 1 set of twins) were born with a median gestation age at delivery of 37 weeks (range 32 – 40 weeks) (Table 1 and 2 and Supplementary Table 1 and 2). Two out of 14 (14%) children with known birth weight were SGA. One neonate was born with tuberous sclerosis complex, a condition inherited from the mother who was diagnosed with RCC during pregnancy (case 2). Another neonate was born with bilateral club feet, after a pregnancy complicated with a TURBT for UCC of the bladder at 28 weeks of gestation. Reasons for neonatal hospitalization were prematurity (n=2), tuberous sclerosis (n=1) and hyperbilirubinemia (n=1). Twins were born after induction of labor at 32 weeks of gestation due to therapy planning for RCC. Both had low birth weight but were in good health.

Oncological outcome

For renal cancer, 15 of 19 patients (79%) with available follow-up were cured and had complete remission. One patient, diagnosed with stage III clear cell RCC, underwent immediate at time of diagnosis a cesarean section at 26 weeks of gestation for placenta previa, followed by radical nephrectomy.¹⁶ One year later she developed lung

metastasis. Another patient died from hemorrhagic shock due to renal cancer rupture as described above.¹⁷ Six years after a diagnosis of stage II RCC, pulmonary metastasis were detected in another patient in early pregnancy. After termination to initiate systemic therapy she progressed rapidly and died 6 months thereafter.¹⁰

For bladder cancer, 13 of 15 patients (87%) with available follow-up had a complete remission. Both patients with stage IV bladder cancer are deceased from disease. Eight months after diagnosis of advanced adenocarcinoma with uterine invasion, one patient suffered from omental metastasis and died a few months later. Another patient underwent a cesarean section followed by a radical cystectomy for a 10-cm bladder mass. She suffered from early disease recurrence in the pelvis with rapid progression and death.²⁵

Comments

Renal cancer

The most common renal cancer type during pregnancy is RCC. In the non-pregnant population, most patients present with a tumor confined to the kidney.²⁹ In this series, over half of pregnant patients were symptomatic and presented with tumors greater than 7 cm (stage II) or advanced (stage III or IV) disease. As clinical presentation might resemble pregnancy-related symptoms, a delayed diagnosis is plausible. It is speculative whether estrogens, who are elevated during pregnancy, might enhance tumor growth in renal cancers. Estrogen receptors are expressed in RCC cells and estrogen is shown to enhance RCC tumor growth in laboratory mice.³⁰ Different studies suggest that parity may increase the risk of developing a renal malignancy.³¹ More research in humans is necessary to confirm this theoretical association.

After urinalysis, abdominal ultrasound should be considered without delay when a pregnant patient presents with loin pain or hematuria. Only consider imaging using

radiation (e.g. Computed tomography (CT)) if results will change management. Below a threshold of 50 mGy no fetal adverse effects are reported, however a pelvic CT potentially exposes the fetus to higher doses and the radiation dose should be estimated in order to define fetal risks.³² Magnetic resonance imaging (MRI) can be considered to differentiate and stage solid renal masses during all trimesters of pregnancy, with the advantage of avoiding fetal radiation exposure.³³ The use of the MRI contrast product, gadolinium, should be limited as it is associated with congenital malformations, nephrogenic systemic malformations and neurotoxic effects.³⁴

Treatment of renal cancer during pregnancy depends on the stage of disease and may be further influenced by the trimester of pregnancy at diagnosis (Figure 2).⁴ Surgery is the gold-standard procedure for the treatment of renal cancer in localized and locally advanced disease and in selected cases with low metastatic burden, especially in the young population.⁴ During the first trimester the transabdominal surgical approach is feasible, whereas in later trimesters the retroperitoneal area is reached by retroperitoneal approach.

RCC's have a slow growing nature with reported doubling times with a range of 300 – 505 days. In case of *a small renal mass (SMR, cT1a, ≤4cm)* a renal biopsy and active surveillance (e.g. every 3 months) might be considered in well selected pregnant patients, according to similar tumor criteria as in the non-pregnant population.³⁵ Strict surveillance during pregnancy seems reasonable as the effect of pregnancy (or increased circulation of estrogens) on the course of renal cancer is still debated.^{30,31}

When *a localized renal mass (cT1b-T2)* is diagnosed during pregnancy, surgical management can be considered if possible.⁴

When a diagnosis is made during the late third trimester, delivery should be planned in order to minimize therapeutic delay. If possible, term delivery (after 37 weeks) is the

goal as a preterm delivery places the child at risk for impaired neurocognitive outcome.³⁶ If delivery is planned by caesarean section, simultaneous oncological surgery is possible.⁴ All cases in this series with a diagnosis after 29 weeks underwent surgical treatment following a delivery beyond 35 weeks, except one twin pregnancy that was induced at 32 weeks.

In patients diagnosed with *locally advanced renal cancer* which invades adjacent structures (T3-4, N+) or *with distant metastasis* (M1) it is suggested to treat regardless of the trimester of pregnancy, as the mother's health should be prioritized.⁴ The parents should be counselled on all treatment options, the fetal risks and potential impact on maternal oncological outcome for all scenarios, including termination of pregnancy or oncological treatment during pregnancy. First trimester exposure to Tyrosine kinase inhibitors (TKI), that can be used in the metastatic setting of renal cancer, is associated with spontaneous abortion and congenital malformations.³⁷ As safety data on the use of TKI (or other targeted or immunotherapy agents) during the second and third pregnancy is still limited to a dozen patients, solid recommendations are not possible at this time.³⁷

In cohort studies including young patients diagnosed with renal cancer, the cancer specific 5-year survival varies between 78-88.4%.²⁹ The maternal outcome in pregnant patients diagnosed with renal cancer seems to be equivalent to that of non-pregnant patients.⁴

Bladder cancer

The most common bladder cancer type during pregnancy is UCC. Patients with bladder cancer usually present with hematuria.⁶ Ultrasound can provide clues, but the

diagnosis in pregnant patients can be missed. Cystoscopy is imperative in the diagnostic work-up of painless hematuria, in the absence of urinary infection.

The treatment during pregnancy depends upon stage of disease and trimester of pregnancy.⁶

Patients diagnosed with *low-risk non-muscle invasive bladder cancer (NMIBC)* [*low grade pTa (diameter < 3 cm)*] can be successfully treated with TURBT followed by a surveillance cystoscopy at 3 months.⁶ Patients with risk factors (pT1 (invasion of the lamina propria), high grade, diameter >3 cm, multifocal, carcinoma in situ) have a high risk of recurrence (up to 45.8%).³⁸ For these cases, immediate post-TURBT instillations or adjuvant therapy by intravesical immunotherapy [Bacillus-Calmette-Guérin (BCG)] or chemotherapy (Mitomycin) might be indicated, according to the guidelines of the European Association of Urology (EAU).³⁵ Local vesical toxicity (e.g. dysuria, frequency) is generally mild and transient, while systemic side effects range from mild symptoms to severe illness (e.g. sepsis, arthritis). Systemic absorption after intravesical administration is limited for most agents as it depends on molecular weight of the drug (very limited if > 300 kDa), but increases with bladder damage (e.g. traumatic catheterization or recent bladder tumor resection). Experience with intravesical treatment during pregnancy is limited to two case reports (BCG and Mitomycin C).^{27,39} Although normal fetal outcomes were reported in each, live vaccines (such as BCG) are contra-indicated during pregnancy and caution is warranted with the use of intravesical Mitomycin as it has the capacity to cross the placenta and is proven embryotoxic in animals.⁴⁰ Therefore, we believe that in intermediate or high risk NMIBC, strict clinical follow-up with (3-monthly) cystoscopy during pregnancy followed by intravesical BCG after pregnancy is reasonable. In patients with *muscle-invasive bladder carcinoma (MIBC)*, *with or without lymph node involvement*, platinum-based

neo-adjuvant chemotherapy is indicated, followed by radical surgery.³⁵ Depending on the gestational age at diagnosis, a termination of pregnancy or initiation of chemotherapy during pregnancy can be considered. With the use of cisplatin dose-dependent neonatal hearing problems are described with doses higher than 70 mg/m².³⁶ Carboplatin seems to be a safer alternative for the fetus. However, cisplatin has proven to be more effective in bladder cancer and fetal risks should be balanced with maternal survival benefits in counselling.³⁵ Also other risks of chemotherapy during pregnancy, including preterm contractions and intra-uterine growth restriction should be discussed.^{36,41} Due to the higher risk of blood loss explained by pelvic congestion, it is suggested to perform radical cystectomy 3-4 weeks after delivery. In case of *metastatic bladder cancer*, treatment options are restricted to palliative chemotherapy. The three patients with advanced bladder cancer in this series were diagnosed in the second trimester of pregnancy and underwent termination or preterm delivery (32 weeks) followed by radical treatment (case 18,19 and Alleemudder et al.).²⁵ Remarkably, one intermediate NIMBC INCIP case (with low grade T1N0) did not receive intravesical treatment postpartum following TURBT in pregnancy (case 15). However the retrospective character of the INCIP registry unavoidably misses or incorporates incorrect data.

Obstetric considerations

Surgery can be performed at any time during the course of pregnancy, however in very early pregnancy (the 2 weeks post conception) the "all-or-nothing" principle applies and patients should be counselled about the risk of early miscarriage.⁴¹ During the late first trimester and the remainder of pregnancy, an adapted anesthetic approach to maximize maternal and fetal safety must be provided, including maintenance of stable oxygenation and blood pressure, avoidance of harmful drugs in early pregnancy,

avoidance of preterm labor and optimal pain control. Spinal anesthesia can be considered as an alternative for general anesthesia. As monopolar TURBT has a higher risk of bladder perforation and other complications (including electrolyte abnormalities), the bipolar technique seems a safer alternative during pregnancy.³⁵ Over the years more cases of laparoscopic (or robotic) interventions for renal cancer during pregnancy are being published.⁴² The advantages of these approaches, such as less blood loss and short hospitalization should outweigh the possible risks such as uterine injury and hemodynamic changes secondary to increased intra-abdominal pressure. A laparoscopic approach can be considered by a surgical team with expertise during the first half of pregnancy (prior to 26 weeks), when the gravid uterus still enables surgical visibility. A priori, patients with urological malignancies can deliver vaginally if there are no other maternal or obstetric contraindications. In bulky tumors the theoretical risk of tumor spread when the neonates passes the birth canal should be discussed with the patient and weighed against the risk of bladder injury and tumor dissemination during caesarean section. In this case series, patients with tumors larger than 4 cm were all delivered by caesarean section.

Treatment goals should include postponement of delivery beyond 35-37 weeks of gestation, whenever possible, in order to safeguard neonatal outcome.³⁶

Conclusions

Despite the rare occurrence of urological cancers during pregnancy, it should be included in the differential diagnosis when a pregnant patient presents with persistent urological complaints. Trimester of pregnancy and stage at diagnosis are most determinant in management. Surgery, if indicated and possible, can be considered safe in all three trimesters and enables term delivery with most optimal neonatal outcome. In the case of unresectable or advanced tumors, mother's health should be

prioritized. If intravesical cytotoxic treatment is indicated, a strict follow-up with cystoscopy during pregnancy followed by postpartum treatment is reasonable, as experience during pregnancy is limited. In summary, urological cancer in pregnancy must be discussed case by case in a multidisciplinary setting, taking both mother's health, neonatal outcome and patient's perspective into account.

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Legends of figures

Figure 1: Management of renal (A) and bladder cancer (B) during pregnancy according to trimester of pregnancy at diagnosis. One miscarriage occurred after a nephrectomy by laparotomy at 7 weeks of gestation. All other pregnancies diagnosed during the first trimester (n=7 for renal cancer and n=5 for bladder cancer), were operated between 10 and 17 weeks of gestation and ended in a live birth.

Figure 2: Recommendations for management of renal (A) and bladder (B) cancer during pregnancy according to stage at diagnosis.

Urological cancers during pregnancy: a report of 22 cases and recommendations for management.

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Table 1: Patient characteristics in renal cancer

	RENAL CANCER					
	Study population (n=14)		Case reports since 2014 (n=15)		All (n=29)	
	Value	%	Value	%	Value	%
Age at diagnosis (years)						
Median (range)	32 (22 – 37)		33 (22 – 46)		32 (22 - 46)	
Parity						
Nulliparous	5	35	3	20	8	28
Multiparous	8	57	6	40	14	48
Not reported	1	7	6	40	7	24
Smoking						
Yes	3	29	0	0	3	10
No	7	50	1	7	8	28
Not reported	4	21	14	93	18	62
Clinical presentation						
Hematuria	1	7	1	7	2	7
Pain	7	50	1	7	8	28
Hypertension	1	7	1	7	2	7
Incidental finding imaging	2	14	10	67	12	41
Persistent UTI	1	7	0	0	1	3
Fever	0	0	1	7	1	3
Hemorrhagic shock	0	0	1	7	1	3
Not reported	2	14	0	0	2	7
Trimester of diagnosis						
First trimester	5	36	5	33	10	34
Second trimester	5	36	8	53	13	45
Third trimester	4	28	2	13	6	21
Obstetric complications						
Hypertension	1	7	1	7	2	7
Pre-eclampsia	1	7	0	0	1	3
Stage at diagnosis						
Stage I	5	36	7	47	12	41
Stage II	5	36	4	27	9	31
Stage III	2	14	3	20	5	17
Stage IV	1	7	1	7	2	7
unknown	1	7	0	0	1	3
Gestational age at diagnosis, weeks (median, range)	18.2 (7 – 30)		16 (6 – term)		16.5 (6-term)	
Maternal outcome						
Complete remission	10	100	5	55	15	79
Recurrent disease	0	0	2	22	2	11
Died due to disease	0	0	2	22	2	11
Lost in follow-up, N/A	4		6		10	
Maternal Follow-up, months (median, range)	33 (9-135)		17 (11 – 96)		30 (3-135)	
Management						
Antenatal treatment	8	57	9	60	17	59
<i>Radical nephrectomy</i>	4	50	4	44	8	47
<i>Partial nephrectomy</i>	4	50	4	44	8	47
<i>Exploratory surgery</i>	0	0	1	11	1	6
Postnatal treatment	6	43	6	40	12	41

Table 2: Patient characteristics in bladder cancer

	BLADDER CANCER					
	INCIP Study population (n=8)		Case reports since 2004 (n=10)		All (n=18)	
	Value	%	Value	%	Value	%
Age at diagnosis (years) Median (range)	32 (28-36)		36 (28-39)		34 (28-39)	
Parity						
Nulliparous	4	50	4	40	8	44
Multiparous	4	50	5	50	9	50
Not reported	0	0	1	10	1	6
Smoking						
Yes	1	12	0	0	1	5
No	5	63	0	0	5	27
Not reported	2	25	10	100	12	67
Clinical presentation						
Hematuria	7	87	4	40	11	66
Incidental finding imaging	1	12	3	30	4	22
Vaginal bleeding	0	0	1	10	1	11
Abdominal pain	0	0	1	10	1	5
Asymptomatic bacteriuria	0	0	1	10	1	5
Trimester of diagnosis						
First trimester	1	12	4	40	5	27
Second trimester	5	63	6	60	11	56
Third trimester	2	25	0	0	2	11
Obstetric complications						
PPROM	0	0	1	10	1	11
Postpartum hemorrhage	1	12	0	0	1	11
Stage at diagnosis						
TaNOM0	2	25	7	70	9	44
Stage I	1	12	0	0	1	5
Stage II	2	25	0	0	2	11
Stage III	1	12	0	0	1	5
Stage IV	1	12	1	10	2	11
unknown	1	12	2	20	3	17
Gestational age at diagnosis, weeks (median, range)	23 (7– 35)		19 (9-26)		21 (7-35)	
Maternal outcome						
Complete remission	6	86	7	87	13	87
Died due to disease	1	14	1	13	2	13
Lost to follow-up	1		2		3	
Maternal follow-up						
Follow-up, months (median,range)	29 (4–197)		6 (1–24)		12 (1-197)	
Management						
Antenatal treatment	4	50	6	60	10	56
TURBT	3	75	4	67	6	60
Partial Cystectomy	1	25	1	17	2	20
Chemotherapy(+TURBT)	0	0	1	17	1	10
Postnatal treatment	4	50	4	40	8	44
Abbreviations: PPRM: Preterm Premature Rupture of Membranes; TURBT: Transurethral resection of the bladder						

Table 3: Pathological characteristics

	Study population		Case reports		All	
Pathological Characteristics	No	%	No	%	No	%
RENAL CANCER						
Renal cell carcinoma	11	79	14	93	25	86
<i>Clear Cell</i>	7	64	6	43	13	52
<i>Papillary type</i>	0	0	3	21	3	12
<i>Chromophobe</i>	3	27	3	21	6	24
<i>Translocation type</i>	0	0	1	7	1	4
<i>Not reported</i>	1	9	1	1	2	8
Nephroblastoma	1	7	0	0	1	3
Not reported	2	14	1	7	3	10
BLADDER CANCER						
Urothelial cell carcinoma	6	75	7	70	13	72
Adenocarcinoma	2	25	1	10	3	17
Squamous cell carcinoma	0	0	2	20	2	11

Table 4: Obstetrical outcome in renal cancer

	RENAL CANCER					
	INCIP study population* (n=13)		Case reports (n=15)		All (n=28)	
	No.	%	No.	%	No.	%
Gestational age at delivery, weeks (median, range)	38 (24 – 39)		35 (26 – 40)		37 (24 - 40)	
Obstetrical outcome						
Live birth	10	71	10	83	20	80
Termination	1	7	1	8	2	8
Miscarriage	1	7	0	0	1	4
Still birth	1	7	1	8	2	8
Not reported	0		3		3	
Live births**						
At term	5	71	4	40	9	53
< 37 weeks	2	29	4	40	6	35
< 32 weeks	0	0	1	10	1	6
< 28 weeks	0	0	1	10	1	6
Not reported	3		0		3	
Onset of labor**						
Spontaneous	4	40	4	40	8	40
Planned delivery	6	60	6	60	12	60
Mode of delivery**						
Vaginal	7	78	6	60	13	68
Elective Cesarean section	2	22	4	40	6	32
Not reported	1		0		1	
Neonatal characteristics**						
Neonatal outcome known	7		2		9	
Birth weight, median (range)	2770 (2240–3700)		(1024-2150)		/	
Percentile, median(range)	69 (1 – 95)		(8-91)		/	
SGA	1	14	1	50	2	22
Congenital malformations	0	0	0	0	0	0
Admission to NICU	2	28	N/A		2	22
* One twin pregnancy excluded						
** only live births included						

Table 5: Obstetrical outcome in bladder

	BLADDER CANCER					
	INCIP study population (n=8)		Case reports* (n=8)		All (n=16)	
	No.	%	No.	%	No.	%
Gestational age at delivery, weeks (median, range)	36 (15 – 40)		38 (18 – 40)		37 (15 – 40)	
Obstetrical outcome						
Live birth	7	88	7	100	14	93
Termination	1	12	0	0	1	7
Not reported	0		1		1	
Live births **						
At term	3	43	5	71	8	50
< 37 weeks	3	43	2	29	5	31
< 32 weeks	1	14	0	0	1	6
Onset of labor**						
Spontaneous	2	29	2	29	4	29
Induction of labor	5	71	5	71	10	71
Mode of delivery**						
Vaginal	3	43	3	43	6	43
Elective Cesarean section	4	57	2	29	6	43
Emergency Cesarean section	0	0	2	29	2	14
Neonatal characteristics**						
Neonatal outcome known	7		3		10	
Birth weight, median (range)	2845 (1700-3685)		3200 (2840-3900)		3315 (1700-3900)	
Percentile, median (range)	44 (3 – 71)		32 (31 – 70)		55 (3 - 80)	
SGA	1	14	0	0	1	10
Congenital malformations	1	14	0	0	1	10
Admission to NICU	2	29	0	0	2	20
* Two twin pregnancies excluded						
** Only live births included						

Figure 1: Management of renal (A) and bladder cancer (B) during pregnancy according to trimester of pregnancy at diagnosis

70 **Figure 2: Timing of delivery (weeks of gestation) according to management during pregnancy for**
71 **renal or bladder cancer.** Only singleton live births with known obstetric outcome included (n=31)
72 Term delivery = delivery after 37 weeks

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Figure 3: Recommendations for management of renal (A) and bladder (B) cancer during pregnancy according to stage at diagnosis.

A. Renal Cancer

Small Renal Mass (T1a)	Consider strict follow-up every three months Surgery after delivery
Localised (T1b-T2)	Surgery during pregnancy <i>If diagnosis in third trimester pregnancy:</i> strict follow-up and surgery after (preferably term) delivery
Locally advanced (T3-T4) or Metastatic (M+)	Prioritise mother's health and treat regardless trimester of pregnancy

B. Bladder Cancer

Non-Muscle Invasive Bladder Cancer (Ta-T1)	<i>Low risk</i> TURB <i>Intermediate/high risk</i> TURB +/- adjuvant treatment if indicated
Muscle Invasive Bladder Cancer (T2-T4, N+)	Consider neo-adjuvant chemotherapy during pregnancy followed by radical cystectomy after delivery
Metastatic (M+)	Palliative Chemotherapy