Maternal and obstetrical outcome in 35 cases of well-differentiated thyroid cancer during pregnancy.

Jan Boucek MD, PhD[a*]; Jorine de Haan MD[b,c*]; Michael J. Halaska MD, PhD[d]; Jan Plzak MD, PhD[a]; Kristel Van Calsteren MD, PhD[e]; Christianne J.M. de Groot MD, PhD[c]; Karina Dahl Steffensen MD, PhD[f]; Robert Fruscio MD, PhD[g]; Elske T. Massolt MD[h]; Philipp Klaritsch MD[i]; Paolo Zola MD, PhD[j]; Frédéric Amant MD, PhD[b,k,l]. *On behalf of the International Network on Cancer, Infertility and Pregnancy (INCIP).*

** Contributed equally*

[a] Department of Otorhinolaryngology, Head and Neck Surgery, The First Faculty of Medicine, Charles University in Prague, University Hospital Motol, V Uvalu 84, 150 06 Prague 5, Czech Republic

[b] Department of Oncology, KU Leuven, Herestraat 49, 3000 Leuven, Belgium

[c] Department of Obstetrics and Gynaecology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands

[d] Department of Obstetrics and Gynaecology, 3rd Medical Faculty, Charles University and Faculty Hospital Kralovske Vinohrady, Šrobárova 1150/50, 100 34, Prague 10 , Czech Republic

[e] Department of Obstetrics and Gynaecology, University Hospitals Leuven, and Department of Reproduction and regeneration, KU Leuven, Herestraat 49, 3000 Leuven, Belgium

[f] Department of Clinical Oncology, Vejle Hospital, Kabbeltoft 25, DK-7100 Vejle, Denmark and Institute of Regional Health Research, University of Southern Denmark, Winsløwparken 19,3, DK-5000 Odense C, Denmark

[g] Clinic of Obstetrics and Gynaecology, University of Milan-Bicocca, San Gerardo Hospital, Via Pergolesi, 33, 20900 Monza, Italy

[h] Department of Endocrinology, Rotterdam Thyroid Center, Erasmus MC, 's-Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands

[i] Division of Obstetrics and Maternal Fetal Medicine, Department of Obstetrics and Gynaecology, Medical University of Graz, Auenbruggerplatz 14, 8036 Graz, Austria

[j] Department of Surgical Sciences, University of Turin, Via Giuseppe Verdi 8, 10124 Turin, Italy

[k] Division of Gynaecologic Oncology, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium.

[l] Center for Gynaecologic Oncology Amsterdam, Antoni van Leeuwenhoek-Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

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Correspondence:

F. Amant, MD, PhD

Center for Gynaecologic Oncology Amsterdam

Antoni van Leeuwenhoek-Netherlands Cancer Institute

Plesmanlaan 121

1066 CX Amsterdam

The Netherlands

Email: f.amant@nki.nl

Phone: +31 20 512 29 75

Fax: +31 20 512 61 50

Abstract

Objective

Thyroid cancer, with 6-10% of cancer diagnoses, is one of the most common malignancies during pregnancy. Its treatment poses a risk for the pregnancy, as the thyroid gland plays a crucial role in the evolution of pregnancy. The aim of this study is to evaluate treatment of primary well-differentiated thyroid cancer during pregnancy and fetal and maternal outcomes..

Study Design

This is an international cohort study

Methods

Primary thyroid cancer patients were identified from the database of the International Network on Cancer, Infertility and Pregnancy registration study. Data on histopathological characteristics, diagnostic and therapeutic interventions, outcome (obstetrical, neonatal and maternal) and maternal follow-up were analysed.

Results

Thirty-five patients with well-differentiated thyroid cancer were eligible. All 35 patients underwent surgery, of which 29 (83%) during pregnancy. Procedures during pregnancy were mainly total thyroidectomies (n=24). Median number of days between diagnosis and surgical treatment was different between the groups with surgery during, and surgery after pregnancy (27 vs 139 days, p<.001). Both maternal and neonatal outcomes were uncomplicated, regardless of gestational age during surgery.

Conclusion

Well-differentiated thyroid cancer diagnosed during pregnancy has a favourable outcome for both mother and child. Surgical management during pregnancy has no negative impact on the pregnancy regardless of the trimester at the time of surgery. However, the potential negative effects of thyroid surgery early in pregnancy demand management of these patients in an experienced multidisciplinary team to provide the best possible care for these patients and their unborn babies.

Keywords: thyroid, cancer, pregnancy, treatment, outcome

Level of Evidence: 4

Introduction

Thyroid cancer is the most frequent endocrine malignancy and occurs in all adult age groups, but affects women two to four times more often than men.[1] In women, the highest incidence occurs between the ages of 30 and 50, making diagnosis during pregnancy not rare.[2-4] Of all cancers diagnosed during pregnancy, thyroid cancer is one of the most common with 6-10% prevalence.[5-8] The prognosis of thyroid cancer in the general population mainly depends on the histopathological subtype and stage of disease at diagnosis. Overall, the prognosis of well-differentiated thyroid carcinoma (WDTC) is favourable, while the behaviour of poorly differentiated or undifferentiated (anaplastic) thyroid carcinoma is very aggressive, leading to a poor outcome.[9-12] The influence of pregnancy on thyroid cancer is still controversial. A few studies describe pregnancy as a negative prognostic factor[13,14], however, larger population based studies do not show a negative impact of pregnancy on the prognosis of WDTC.[3,13,15-17]

The last two decades have seen the proposition of guidelines on the oncological management of these patients that aim to safeguard the pregnancy.[11,18] The obstetrical outcome of pregnant cancer patients is different from the general population with regards to preterm birth and birth weight.[5] Moreover, as the thyroid gland plays a crucial role in the evolution of pregnancy, thyroid cancer treatment during pregnancy poses a risk for the foetus. Obstetrical outcomes of pregnant thyroid cancer patients have mainly been described in case reports and small series. Larger cohorts describe either maternal or obstetrical outcome, or do not specify the treatment during pregnancy.[16,17,19-22]

Therefore, the aim of this international cohort study is to evaluate treatment and subsequent fetal and maternal outcome for pregnant patients with primary WDTC.

Materials and Methods

This study was an international observational cohort study, that used the database of the International Network on Cancer, Infertility and Pregnancy (INCIP) (ClinicalTrials.gov, NCT00330447). The INCIP is a worldwide collaboration on cancer in young women that started in 2005 with a

registration study on pregnant patients with any type of cancer to evaluate oncological care, obstetrical, maternal and neonatal outcome. At the conclusion of our study, the INCIP consisted of 97 members from 83 centres in 30 countries working in hospitals that have experience with cancer during pregnancy. The collaborating physicians included several oncological specialists, obstetricians, neonatologists and paediatricians. Patients were registered both retrospectively and prospectively. Patients were eligible for this study when primary thyroid cancer was confirmed histologically and patients either were pregnant or became pregnant while undergoing active therapy. All required ethical approvals were obtained from all participating centres.

Data collection included demographic features, symptoms, histopathological characteristics, diagnostic and therapeutic interventions, obstetrical characteristics, obstetrical, neonatal and maternal outcome and maternal follow-up.

Results

From June 2004 to October 2016, 40 patients with thyroid cancer during pregnancy were registered in the INCIP database. Three of these patients presented with recurrent thyroid cancer between 3 and 7 years after primary diagnosis. These patients were excluded from this study. Patients were treated in the Czech Republic (Prague n=22), the Netherlands (Amsterdam n=2, Ede n=1, Rotterdam n=1), Italy (Monza n=3, Turin n=2), Belgium (Leuven n=3), Denmark (Vejle n=2), and Spain (Madrid n=1). See Table 1 for the patient characteristics. Median age at diagnosis during pregnancy was 30 years (interquartile range (IQR) 29 - 32 years) with a median gestational age (GA) at diagnosis of $15^{4/7}$ weeks (IQR $9^{1/7}$ – $18^{4/7}$ weeks). Diagnosis occurred during the first (n=14, 38%), second (n=18, 49%) and third (n=2, 5%) trimester. Three patients (8%) became pregnant during treatment.

<u>Diagnostic specifications</u>

A mass in the thyroid region was the most common presentation during pregnancy (n=27, 73%). In six patients (16%), diagnosis resulted from perceived abnormalities in thyroid function tests included

in regular pregnancy check-ups and one (3%) patient presented with cervical lymphadenopathy. For three pregnant patients, the symptoms were unknown at presentation.

Diagnostic high-resolution ultrasound of the neck was performed in 32 pregnant patients and followed by fine needle aspiration cytology (FNAC) of a thyroid lesions, including the patient who presented with cervical lymphadenopathy. Bethesda classification of the FNAC was available in 91% of these patients; one was Bethesda category III, five Bethesda category IV, four Bethesda category V and 19 were Bethesda category VI.[23] Other imaging performed during pregnancy included one magnetic resonance imaging (MRI) of the neck region at a GA of 5 weeks and one positron emission tomography with computed tomography (PET/CT) scan around the time of conception followed by an x-ray of the chest without shielding due to unknown pregnancy, also at a GA of 5 weeks.

Histopathological characteristics

Twenty-four patients (65%) had unilocular thyroid cancer that was located on the left side (n=10), right side (n=8), the isthmus (n=2) or an unknown location (n=4), whereas 13 patients (35%) presented with multilocular cancer (12 with WDTC). Patients were primarily diagnosed with WDTC (n=35, 95%), with papillary thyroid carcinoma (PTC) being the most common subtype (n=30, 81%). Three patients had follicular thyroid cancer (FTC) (8%) and two had a follicular variant of papillary thyroid cancer (5%). All patients with WDTC had stage I disease.[24] Most of these tumours were smaller than 2 cm (T1, n=20, 57%). Five patients (14%) had tumours sized between 2 and 4 cm (T2), eight (22%) had a primary tumour larger than 4 cm without invasion of surrounding tissue (T3) and two (6%) had tumours invading the surrounding tissue (T4). Nine of these patients (26%) had lymph node involvement, and none of the patients with WDTC had distant metastases.

One patient was diagnosed with poorly differentiated medullary thyroid cancer and one with undifferentiated anaplastic thyroid cancer. Both had stage IV disease, one with tumour invasion of the thyroidal fat pad and the other with invasion of the trachea, larynx and strap muscles. For the next part of the manuscript on therapeutic management and obstetrical, neonatal and maternal

outcomes, only patients with WDTC are included. Detailed information on these patients can be found in Table 2.

Therapy

Surgical therapy

All 35 patients underwent surgery, of whom 29 (83%) received their first surgical treatment during pregnancy. Three of these patients were surgically treated both during and after pregnancy, while the remaining six (17%) received surgical treatment only after delivery (Table 3). Of the surgeries during pregnancy, 24 patients (83%) underwent a total thyroidectomy, four (10%) underwent a hemithyroidectomy and one patient (3%) only underwent a lymph node resection.

Eight patients underwent a neck dissection (ND), of which seven were pregnant. In only one of these patients, the ND was prophylactic. All eight NDs included level VI lymph node stations, of whom six were bilateral. Five patients underwent dissection of additional levels, such as levels II to V (unilateral n=3 and bilateral n=1) and levels I to V (n=1).

For all 35 patients with WDTC, median therapeutic interval between diagnosis and first surgical treatment was 35 days (IQR 11-74 days). This interval was 27 days (IQR 10 – 54 days) in patients treated during pregnancy compared to 139 days (IQR 104 – 204) in patients treated postpartum (Mann-Whitney U Test, p<.001). There was no difference in the trimester at time of diagnosis between these groups.

Non-surgical therapy

Twenty-two patients received radioactive iodine (RAI) therapy, though this therapy was always postponed until after pregnancy. The median dose of I-131 was 3700 mega Becquerel (MBq) (IQR 2127 – 3700 MBq). External beam radiotherapy to the neck was applied only once, 51 days after delivery.

Obstetric and neonatal outcome

Of all 35 pregnancies complicated by WDTB, three were terminated and 32 ended in a live birth. Two terminations were performed early in the first trimester with maternal wish for termination after diagnosis of PTC with nodular invasion. The third was performed in the second trimester because of congenital anomalies of the child. Median GA at delivery was $40^{0/7}$ weeks (IQR $38^{5/7}$ – $40^{6/7}$). None of the pregnancies ended preterm. Five deliveries were vaginally induced and five pregnancies ended by elective caesarean section (CS). Three of the inductions were done because of therapy planning; the two other inductions and all CS were because of obstetrical reasons.

Median birthweight was 3390 grams (IQR 3113 - 3562). When adjusted for GA at delivery, sex and parity of the mother, only one child (3%) had a birth weight below the 10th percentile (small-for-gestational-age, SGA) and four (12%) had a birthweight above the 90th percentile. APGAR scores of all children at 5 minutes were 7 or higher. One child was admitted to the neonatal intensive care unit because the onset of icterus within 24 hours after birth and was treated with phototherapy only. Congenital anomalies were not reported in the children born from ongoing pregnancies.

Maternal outcome

Median follow-up was 3.2 years (IQR 1.7 – 6.5 years). All patients with primary WDTC were alive at last follow-up. Disease free survival (DFS) can be seen in Figure 1, three patients had a recurrence after pregnancy, respectively after ten, 14, and 28 months.

Discussion

This study analysed the oncological management and both obstetrical and maternal outcomes of 35 patients with primary WDTC during pregnancy. All patients were diagnosed with stage I disease, with a majority of small (T1) tumours (n=20, 57%) and all patients received therapeutic surgery, of which 83% (n=29) was performed during pregnancy. The median number of days between diagnosis and surgical treatment was significantly shorter in the group who received surgery during pregnancy compared to those who only received surgical treatment after pregnancy (27 vs 139, p<.001). There

was no difference in trimester at the time of diagnosis between these two groups. Thirty-two (91%) pregnancies ended in a live birth, all carried to full term. Both maternal and neonatal outcome was favourable.

Diagnostic procedures

In patients with palpable masses or suspected lesions on ultrasound, additional high-resolution ultrasound guided FNAC should be performed to histopathologically confirm disease. High-resolution ultrasonography of the thyroid gland in combination with FNAC is the examination of choice as it has a high sensitivity (up to 97%) and specificity (up to 98%) when performed by an experienced person.[25-30] For those of our patients with a Bethesda score available, 97% indicated a highly suspicious or proven malignant tumour, which is a comparable accuracy to the one reported above.

Other imaging techniques performed in our population during pregnancy to exclude distant metastasis, were MRI of the neck region (n=1) and a PET/CT scan with additional x-ray of the chest (n=1). CT scan of the upper body is safe to perform during pregnancy and poses little to no fetal radiation exposure in the first and second trimester of pregnancy.[31] As for the use of ^{18}F-FDG PET/CT scans, the diagnostic accuracy in thyroid cancer appears to be similar to that of ultrasound with FNAC and is not standard care in the diagnostic process of thyroid gland pathology. A PET scan during pregnancy does not expose the fetus to high levels of radiation (2.7×10^{-2} – 9.4×10^{-3} mGy/MBq), but nuclear-labelled tracers are non-equally distributed in the fetus, with the brain resorbing the most. Theoretically, short and long term neurological development could be impaired.[31,32] Therefore, especially during pregnancy, PET/CT scans should be reserved for cases with a high risk of distant metastases, where no other diagnostic techniques are available, and where management and maternal outcome depend on it.

Histopathological characteristics

As in non-pregnant women in the fertile age, the majority of primary thyroid tumours in our database were WDTC (95%) – papillary (n=30), follicular carcinoma (n=3) and follicular variant of papillary carcinoma (n=2). WDTC was multifocal in 12 patients (34%). It is important to consider multifocality when deciding on the extent of surgical therapy, because it is a sign of tumour aggressiveness and is associated with an increased risk of lymph node metastasis and recurrent disease.[11,33-35] This is also found in our series, where 42% (n=5) of the patients with a multifocal tumour had tumour invasion outside the thyroid.

Treatment

Surgical treatment

Currently, general consensus states that in pregnant thyroid cancer patients, surgery can be postponed until after pregnancy in patients with no evidence of advanced disease or rapid progression.[18,36] Alternatively, second trimester total thyroidectomy is advised.[18,36] The majority of patients underwent surgical therapy during pregnancy (n=29, 83%). Most of them were diagnosed in the first (n=12) or second (n=14) trimester. Ninety-three percent of the patients diagnosed in the first trimester, and 82% of the patients diagnosed in the second, received surgery during pregnancy. Of all 29 patients that had surgery during pregnancy, 20 had WDTC (T<3N0) and postponement of surgery until after delivery would have been an option based on the current general consensus. Non-obstetrical surgery in pregnant patients has, however, been described to be safe in all trimesters and pregnant women with cancer should be treated as non-pregnant cancer patients where possible.[18,36] Furthermore, delaying primary treatment until after delivery can cause an extra psychological burden and stress for the mother, especially when diagnosed in the first trimester and the time between diagnosis and treatment is substantial.

Obstetrical outcome

Obstetrical outcome in our cohort was good, with 91% ongoing pregnancies and no increase in the number of obstetrical or neonatal complications, regardless of the trimester of diagnosis or surgery. This is presumably due to the high number of stage I and localized disease, resulting in standard treatment, limited to surgery. In our population, no obstetrical adverse effects of surgery during pregnancy were observed. The percentage of SGA children (3%) was not higher than that of the general population (5-10%).[37] These findings are in agreement with previously published articles.[19,22]

Maternal outcome

The prognosis of thyroid cancer depends on the primary histological type of the disease and on the age of the patient.[38] For WDTC the outcome is favourable, especially in young patients. In addition, no negative effect of pregnancy on the OS of thyroid cancer patients has been observed which is in line with our findings.[3,6,16,17] We found no increased risk for recurrent disease in our population. oOly two studies showed a negative effect of pregnancy on DFS and persistent disease, but it has been suggested that these studies used more sensitive markers for recurrence and/or persistence of disease.[6,13,39] Moreover, both studies included postpartum diagnosis, which could be also explain the differing results.[13] Andersson et al. reported a lower number of thyroid cancer patients diagnosed during pregnancy than what would be expected in the non-pregnant population. They also observed a subsequent increase of thyroid cancer diagnosis in the postpartum period. This might have resulted in a higher tumour load at the time of diagnosis, possibly resulting in a worse outcome.[40]

Limitations of this study

This study in one of few studies focussing on oncological, as well as obstetrical and neonatal outcome. We are aware that our numbers are relatively small. This is inherent to the subject of cancer during pregnancy overall, and even more so for thyroid cancer during pregnancy, specifically. Ideally, management of thyroid cancer patients during pregnancy should be performed in, or in collaboration with, an academic centre. INCIP members are mostly affiliated to academic hospitals,

however, registration of these cases in our international network was on a voluntary basis and we cannot guarantee that all patients were included. It is possible that patients with low stage disease or diagnosis at the end of pregnancy refrained from consulting an academic centre. In our population, the majority of patients had stage I disease, making it less plausible that our population is subset to such selection bias and our observed distribution of disease stage and maternal outcome is comparable to the literature. Moreover, by retrospectively including historical data, we were able to complete the dataset on overall exposure to thyroid cancer during pregnancy of one hospital. We therefore believe that our data are valid and gives a good overview of the maternal and obstetrical outcome of pregnant patients with primary WDTC.

Conclusion

WDTC is the most common type of thyroid cancer diagnosed during pregnancy, and has a favourable outcome. Postponing surgical management until after delivery significantly increases the interval between diagnosis and treatment, with possible adverse effects on maternal well-being. The outcome of pregnancy in pregnant thyroid cancer patients was favourable and neonatal outcome was similar to the general population. Due to multiple individual factors that may negatively influence maternal and/or neonatal outcome, however, management of these patients must involve an experienced multidisciplinary team in order to provide the best possible care for these patients and their unborn children.

Details of ethics approval

Ethical approval was obtained in those centres where needed.

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Figure Legends

Figure 1. Disease free survival after diagnosis of primary thyroid cancer during pregnancy.

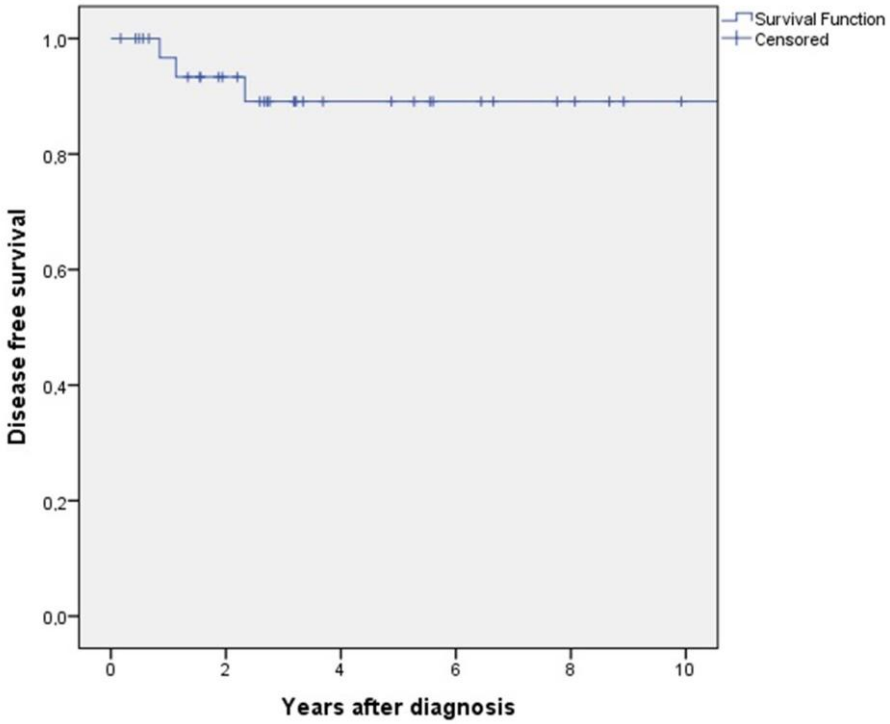

Table 1. Patient characteristics.

	Median	**IQR**
Age at diagnosis	30	29 – 32
Gestational age at diagnosis	$15^{4/7}$	$9^{1/7}$ – $18^{4/7}$
	No.	**%**
Trimester of diagnosis		
- First trimester	14	38
- Second trimester	18	49
- Third trimester	2	5
- Pregnant during therapy	3	8
Stage of disease during pregnancy		
- Stage I	35	94
- Stage IVA	1	3
- Stage IVB	1	3
Therapy management during pregnancy		
- No therapy	7	19
- Surgery alone	29	78
- Surgery + Radiotherapy	1	3

Table 2. Clinical and histopathological characteristics, treatment during and after pregnancy, fetal- and maternal outcome of all patients with primary WDTC.

Case	Symptoms	Focality	Subtype	TNM	Age at diagnosis	GA at diagnosis	Treatment during pregnancy	Treatment after pregnancy	Fetal outcome (GA at delivery, delivery mode, birth weight, NICU admissions)	Maternal outcome (FU, Recurrent disease, DFS)
1	Unknown	Multi	Papillary	T1NXMX	27	$12^{5/7}$	Total thyroidectomy		Live birth, $40^{6/7}$ weeks, Vaginal delivery, 3050 g	NED after 5,3 years
2	Asymptomatic	Multi	Papillary	T1N0M0	30	$9^{4/7}$	Total thyroidectomy		Live birth, $40^{3/7}$ weeks, Vaginal delivery, 3360 g	NED after 5,6 years
3	Tumour in the neck	Multi	Papillary	T1N1M0	30	$26^{1/7}$	Total thyroidectomy + Neck dissection	Iodine-131 therapy	Live birth, $39^{5/7}$ weeks, Vaginal delivery, 3640 g	NED after 4,9 years
4	Tumour in the neck	Single	Papillary	T1N0M0	29	$17^{6/7}$	Total thyroidectomy		Live birth, $40^{0/7}$ weeks, Vaginal delivery, 3450 g	NED after 2,8 years
5	Unknown	Multi	Follicular	T3NxM0	30	Pregnant during therapy	Hemithyroidectomy	Total thyroidectomy + Iodine-131 therapy	Live birth, $41^{4/7}$ weeks, Vaginal delivery	NED after 3,2 years
6	Unknown	Multi	Papillary	T4N1M0	39	$3^{4/7}$	Total thyroidectomy + Neck dissection	Iodine-131 therapy	Live birth, $38^{6/7}$ weeks, Vaginal delivery, 3800 g	NED after 0,5 years
7	Tumour in the neck	Multi	Papillary	T1N0M0	28	$15^{5/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $40^{4/7}$ weeks, Vaginal delivery, 3510 g	NED after 3,3 years
8	Tumour in the neck	Single	Papillary	T1N0M0	35	$29^{1/7}$		Total thyroidectomy	Live birth, $40^{0/7}$ weeks, Caesarean section	NED after 2,6 years
9	Tumour in the neck	Multi	Papillary	T2N1M0	30	$6^{3/7}$	Total thyroidectomy + Neck dissection	Iodine-131 therapy	TOP	NED after 7,8 years
10	Tumour in the neck	Single	Follicular	T2N0M0	29	$13^{6/7}$	Nodus resection	Total thyroidectomy + Iodine-131 therapy	Live birth, $37^{5/7}$ weeks, Vaginal delivery, 3485 g	NED after 1,6 years
11	Tumour in the neck	Single	Papillary	T2N1Mx	26	$15^{6/7}$	Total thyroidectomy + Neck dissection	Iodine-131 therapy	Live birth, $38^{6/7}$ weeks, Caesarean section	NED after 0,7 years
12	Asymptomatic	Single	Papillary	T1N0M0	36	$15^{6/7}$		Total thyroidectomy	Live birth, $39^{1/7}$ weeks, Vaginal delivery, 3150 g	NED after 2,7 years
13	Tumour in the neck	Single	Papillary	T1N0M0	30	$17^{3/7}$		Hemithyroidectomy + Total thyroidectomy +	Live birth, $40^{0/7}$ weeks, Caesarean section	RD after 1,1 years

								Iodine-131 therapy		
14	Tumour in the neck	Single	Follicular	T3N0M0	32	$9^{6/7}$	Hemithyroidectomy	Total thyroidectomy + Iodine-131 therapy	Live birth, $42^{0/7}$ weeks, Vaginal delivery, 4650 g, NICU admission due to icterus <24 hrs after birth	NED after 2,2 years
15	Asymptomatic	Single	Papillary	T1N0M0	32	$17^{3/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $37^{4/7}$ weeks, Vaginal delivery, 3330 g	NED after 2,7 years
16	Asymptomatic	Single	Papillary	T1N0M0	29	$19^{1/7}$	Total thyroidectomy		Live birth, $41^{3/7}$ weeks, Vaginal delivery, 3910 g	NED after 3,2 years
17	Asymptomatic	Single	Papillary	T3N1M0	29	$25^{3/7}$		Total thyroidectomy + Neck dissection	Live birth, $37^{0/7}$ weeks, Vaginal delivery, 2730 g	NED after 5,6 years
18	Tumour in the neck	Single	Papillary	T3N1M0	29	Pregnant during therapy		Total thyroidectomy + External beam radiotherapy	TOP	RD after 2,3 years
19	Tumour in the neck	Single	Papillary	T2N1Mx	28	$29^{4/7}$	Total thyroidectomy + Neck dissection		Live birth, $40^{4/7}$ weeks, Vaginal delivery, 3770 g	RD after 0,9 years
20	Tumour in the neck	Single	Papillary	T3N0M0	33	$17^{2/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $39^{6/7}$ weeks, Vaginal delivery, 3100 g	NED after 8,9 years
21	Tumour in the neck	Single	Papillary	T1N0M0	30	$9^{5/7}$	Total thyroidectomy + Neck dissection		Live birth, $38^{6/7}$ weeks, Vaginal delivery, 3330 g	NED after 9,9 years
22	Tumour in the neck	Multi	Papillary	T3N0M0	29	$26^{5/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $39^{1/7}$ weeks, Vaginal delivery, 3090 g	NED after 10,8 years
23	Tumour in the neck	Single	Papillary	T1N0M0	36	$13^{2/7}$	Total thyroidectomy		Live birth, $40^{2/7}$ weeks, Vaginal delivery, 3580 g	NED after 3,2 years
24	Tumour in the neck	Single	Papillary	T1N0M0	30	$8^{5/7}$		Total thyroidectomy + Iodine-131 therapy	TOP	NED after 8,1 years
25	Tumour in the neck	Single	Papillary follicular	T1N1M0	38	$7^{4/7}$	Total thyroidectomy + Neck dissection	Iodine-131 therapy	Live birth, $39^{5/7}$ weeks, Vaginal delivery, 3380 g	NED after 0,2 years
26	Tumour in the neck	Single	Papillary	T2N2M0	30	$15^{4/7}$	Total thyroidectomy		Live birth, $40^{0/7}$ weeks, Vaginal delivery, 3500 g	NED after 3,7 years
27	Tumour in the neck	Single	Papillary	T1N0M0	30	$18^{0/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $38^{5/7}$ weeks, Vaginal delivery, 3960 g	NED after 6,7 years

28	Tumour in the neck	Multi	Papillary follicular	T3N0M0	25	$6^{6/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $38^{3/7}$ weeks, Caesarean section, 2860 g	NED after 8,7 years
29	Tumour in the neck	Single	Papillary	T2N0M0	32	$17^{2/7}$	Hemithyroidectomy	Iodine-131 therapy	Live birth, $37^{1/7}$ weeks, Caesarean section, 3400 g	NED after 1,4 years
30	Tumour in the neck	Multi	Papillary	T3N0M0	30	$11^{0/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $41^{1/7}$ weeks, Vaginal delivery, 3000 g	NED after 1,9 years
31	Tumour in the neck	Single	Papillary	T1N0M0	29	$19^{6/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $41^{4/7}$ weeks, Caesarean section, 3340 g	NED after 1,9 years
32	Tumour in the neck	Multi	Papillary	T1N0M0	29	$21^{3/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $41^{3/7}$ weeks, Vaginal delivery, 3500 g	NED after 1,5 years
33	Tumour in the neck	Single	Papillary	T1N0M0	22	$11^{1/7}$	Total thyroidectomy		Live birth, $38^{5/7}$ weeks, Vaginal delivery, 3330 g	NED after 6,4 years
34	Tumour in the neck	Multi	Papillary	T1N0M0	33	$2^{0/7}$	Total thyroidectomy	Iodine-131 therapy	Live birth, $41^{1/7}$ weeks, Vaginal delivery, 3510 g	NED after 0,4 years
35	Asymptomatic	Single	Papillary	T1N0M0	33	$22^{3/7}$	Hemithyroidectomy		Live birth, $38^{1/7}$ weeks, Vaginal delivery, 2920 g	NED after 0,6 years

GA; gestational age, NICU; neonatal intensive care unit, FU; follow up, DSF; disease free survival, NED; no evidence of disease, RD; recurrence of disease

Table 3. Treatment modalities performed during pregnancy and postpartum for patients with primary WDTC.

During pregnancy	**No.**	**%**	**Median GA**	**IQR range**
Surgery	29	83		
- Hemithyroidectomy	4	14	$18^{3/7}$	$7^{2/7} – 23^{2/7}$
- Total thyroidectomy	24	83	$20^{1/7}$	$18^{5/7} – 24^{3/7}$
- Neck dissection	7	24	$17^{0/7}$	$7^{5/7} – 27^{5/7}$
- Diagnostic lymph node excision	1	3	$13^{6/7}$	NA
Postpartum			**Median weeks**	**Range**
Surgery	9*	26		
- Hemithyroidectomy	1	11	6	NA
- Total thyroidectomy	9**	100	7	6 – 21
- Neck dissection	1	11	6	NA
Radioiodine therapy	22	63	22	11 – 67
External beam radiotherapy	1	0	7	NA

* Three patients underwent both surgery during and after pregnancy.

** One patient underwent additional surgery after hemithyroidectomy with tumour invaded margins.