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EARLY DETERMINANTS OF THYROID FUNCTION OUTCOME IN CHILDREN WITH CONGENITAL HYPOTHYROIDISM AND A NORMALLY LOCATED THYROID GLAND: A REGIONAL COHORT STUDY

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An increase in the incidence of congenital hypothyroidism (HC) has been shown in recent years in various countries, including France. This increase in incidence affects mainly patients with normally located gland while the incidence rate of thyroid dysgenesis remains stable^{1,2}. The national study that we carried out in collaboration with the French Association for the Screening and Prevention of Child Disabilities (AFDPHE) and Public Health France showed that neither the modifications of the TSH screening threshold, regional differences methods of assay (Delphia, RIA), prematurity, analysis of the variables collected during the HC screening could currently explain the increase in the incidence rate of congenital hypothyroidism with a normally located thyroid gland³. Two studies carried out in Ile de France showed a tendency to increase the transient forms of 38 to 56% on these studies, but those studies were limited in number with (many lost to follow-up, but conducted respectively before 2002 and between 2005 and 2008^{4,5}).

The currently reported etiologies of transient forms mainly include iodine overload or, on the contrary, iodine deficiency, transplacental passage of maternal blocking antibodies on thyroid function (maternal thyroiditis), or synthetic antithyroidism (Graves' disease). mother treated during pregnancy) and some forms of disorders of thyroid hormone synthesis (THOX2 genes, TSH-R, Pendred syndrome, trisomy 21). An association between serum TSH concentrations at the upper limit of normal and minor neurodevelopmental abnormalities at 5-10 years of age has recently been reported by an Australian team⁶. These results highlight the need for vigilance in the management of these patients. The objective of this study was to describe the evolution of congenital hypothyroidism with normally located gland in order to evaluate the current proportion of transient versus permanent forms, to describe the characteristics of these two evolutionary forms, and to try to identify explanatory factors for permanent versus transitory identity.

This is a monocentric observational study of all patients detected between 2002 and 2012 in the sector of the Robert Debré University Hospital (CEERB N° 2016/319). Of the 240 patients screened during this period, 110 (46%) had an abnormality of gland development (athyreosis n = 34, ectopy n = 76) and 130 (54%) had a gland in place. Of the patients with glands in place, 31 patients had a transient untreated hyper-TSH, and treatment with Levothyroxine was instituted in 99 patients. During the evolution, the re-evaluation of the thyroid function could not be realized in 7 patients (n = 2 deaths, n = 5 lost to follow up).

Data collection included the study of family history of HC, characteristics of patients at birth and at the time of initial evolution, with morphology of the gland, scintigraphy data, thyroxine L dose (LT4), depending on the transient or permanent nature, as well as the evolution of thyroid function and treatment.

The form of transient hypothyroidism was defined as normal thyroid function with normal serum TSH (<7 mIU / L) after interrupted treatment for at least 4 weeks. Patients were considered to have a permanent form if serum TSH was elevated (> 7 mIU / L) during treatment, during a decrease or discontinuation of treatment. The total duration of treatment for patients with transient form was collected. It is important to note that there was no specific protocol for stopping thyroid replacement therapy for re-evaluation, which was left open to the clinician's judgment.

Results: Of the 92 patients with HC with normal gland, 49 (54%) patients had a transient form and 43 (46%) patients with permanent form. Multivariate analysis of the variables associated with a transient form made it possible to show that the presence of a form of familial HC was associated with the evolution towards a permanent form (OR = 0.06 (0.00-0.66), p <0.02), and that low doses of Levothyroxine at 6 months of age were associated with a transition to a transient form (p <0.001). A treatment threshold value of 3.2 µg/kg/day was associated with a sensitivity of 71% and specificity of 79% (area under the ROC 0.83 curve). However, neither the initial severity of HC (assessed on serum TSH, T4L, the presence or absence of ossification points), gender, neonatal antecedents (prematurity, IUGR, neonatal distress), and the morphology of the thyroid gland was associated with the evolutionary risk (permanent form versus transient).