Congenital Hypothyroidism in Newborn Infants with Borderline TSH Screening Cut-off Points

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CONGENITAL HYPOTHYROIDISM (CH)

- Congenital Hypothyroidism (CH) is one of the most preventable causes of intellectual disability

- Philippine data (as of Dec 2014) ¹
  - Incidence is 1 in 2,673

- Screening for CH started in 1996 ¹

- Biomarker – elevated TSH on DBS sample collected (heel-prick method)

¹. Newborn Screening Reference Center, National Institutes of Health, University of the Philippines, Manila, December 2014.
5 Newborn Screening Centers (NSCs) in the Philippines

NSC – Southern Daniel Mercado Medical Center (Region 4)

NSC – Central Luzon (Angeles University Foundation) Regions 1, 2, 3 & CAR

NSC – Mindanao (Southern Philippines Medical Center) Regions 9, 10, 11, 12, 13 & ARMM

NSC – Visayas (West Visayas State University) Regions 6, 7, & 8

NSC – NIH (Ayala Technohub) NCR, Region 5

TSH Cut-off Value
$\geq 15 \text{ mIU/L}$

TSH Cut-off Value
$\geq 12.5 \text{ mIU/L}$
CH SCREENING ALGORITHM

TSH <10 mIU/L
NFT - No Further Test

TSH ≥ 10 mIU/L
Retest in duplicates (AB)

TSH1
> 12.5-14.5 mIU/L
if <10d

TSH1
> 15-99 mIU/L
if <10d

TSH2
> 12.5-14.5 mIU/L
if >10d

TSH2
> 15-99 mIU/L
if >10d

TSH2
> 100 mIU/L

TSH 1 – repeat NBS test
TSH 2 – confirmatory testing, pediatric endocrinologist referral
OBJECTIVE

➢ To evaluate the clinical outcome of newborn infants who initially had borderline TSH screening result and were subsequently confirmed to have CH when further examination was carried out
MATERIALS & METHOD

- Retrospective study

- Data review of newborn infants screened between January 2011 to December 2014 and who had borderline TSH screening values (≥12.5-14.5 mIU/L) and subsequently confirmed to have CH

- Data include:
  - Demographics (including screening & treatment age)
  - Laboratory number, TSH values (initial & repeat)
  - Relevant investigations done (serum TSH, FT4 & imaging studies)
RESULTS

786,175 Neonates screened (2011-2014)

784,661 (99.81%)
TSH <12.5 mIU/L
NFT

1,514 (0.19%)
TSH > 12.5 mIU/L

401 (26%)
TSH ≥ 12.5 – 14.9 mIU/L
BORDERLINE

884 (58%)
TSH ≥ 15-99 mIU/L
TSH1

229 (15%)
TSH >100 mIU/L
TSH2

TSH 1 – repeat NBS test
TSH 2 – confirmatory testing, pediatric endocrinologist referral
RESULTS

401 Neonates
TSH > 12.5 – 14.5 mIU/L
BORDERLINE

396 (98.75%)
< 10 days old – (TSH 1)

363 NFT
1 Expired
1 LTFU

31 TSH2
15-80 mIU/L

3 Confirmed CH

5 (1.25%)
>10 days old - (TSH 2)

2 NFT

6 NFT
1 Transient CH
1 LTFU

23 Confirmed CH
RESULTS

26 Confirmed CH:

15 males (57.7%)
11 females (42.3%)
All were full term babies (38-40 weeks)

Median screening age 2 days
Median age of treatment - 28.5 days

8 babies were clinically symptomatic – umbilical hernia, prolonged jaundice
26 Confirmed CH:

- serum TSH values ranged from $8.35 - 85$ (NV $0.25-5$ uIU/ml)
- serum FT4 values ranged from $1.60 – 8.34$ (NV $9-20$ pmol/L)
- 8 cases had low normal serum FT4 values $11 – 14$ (NV $9-20$ pmol/L)

Antibodies & iodine status were not determined (not readily available in the local setting)

Only 4 underwent imaging studies (because of financial limitations)
RESULTS

26 Confirmed CH:

- with normal growth & development
- are still on treatment (at present date)
- still following up at the NBS continuity clinic
NBS Continuity Clinics

14 Continuity Clinics in operation

RECALL RATE 77%

(Each of continuity clinics has a full time nurse & a part time pediatrician)

- Ilocos Training and Regional Medical Center, Region 1
- Cagayan Valley Medical Center, Region 2
- Jose B. Lingad Memorial Regional Hospital, Region 3
- Baguio General Hospital and Medical Center, CAR
- Philippine General Hospital, NCR
- Gen. Emilio Aguinaldo Memorial Hospital, CALABARZON
- Bicol Regional Training and Teaching Hospital, Region 5
- West Visayas State University Medical Center, Region 6
- Vicente Sotto Memorial Medical Center, Region 7
- Eastern Visayas Regional Medical Center, Region 8
- Zamboanga City Medical Center, Region 9
- Northern Mindanao Medical Center, Region 10
- Southern Philippines Medical Center, Region 11
- Cotabato Regional Medical Center, Region 12
DISCUSSION

- CH screening highly successful

- Screening protocols for CH differ in many NBS programs e.g. analyte cut-off points

- Some programs adopt lower cut-off points to avoid missed cases

- Using borderline TSH cut-off points has increased detection rate of CH including subclinical CH

- The 26 true & subclinical CH would have been missed cases had NSC Mindanao used the >15 uIU/L TSH cut-off points.
DISCUSSION

- Impact of treating subclinical CH remains to be seen.
- Some studies show that children with subclinical CH are at risk for overt hypothyroidism later in life % will therefore benefit from levothyroxine treatment.  

- Grosse et al study – children with subclinical CH documented a decreased intellectual potential & increased behavioral abnormalities.  

- Need to monitor subclinical cases.
DISCUSSION

- Lowering cut-off points will lead to increased recall rate.
- Using the recommended screening cut-off points, recall rate was 0.14%.
- With lower cut-off, recall rate was 0.19%.
The use of borderline TSH cut-off points has increased the detection rate of both true and subclinical CH.

TSH screening cut-off point may be lowered to >12.5 mIU/L for appropriate screening outcome and to avoid missing any case of CH.
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