[6]. In pre-pubertal children, IIH appears to be even less frequent;we found three girls and three boys each in the pre-pubertal age. Children with IIH are reported to have an equal sex distribution [7], though we found a male female ratio of 1:2. Affected adolescents of IIH tend to be overweight, but obesity and weight gain do not appear to be risk factors [8]. In our series one girl was obese, two were overweight; one of whom was in pubertal age. Acute headache and double vision were the common symptoms on initial presentation and none of our patients were picked upon routine examination. We had three patients with sixth nerve palsy as false localizing sign, who presented with sudden squinting.

Visual loss has been reported to occur in children with IIH. Pediatric IIH is just as threatening to vision as the adult form [6], in our study we encountered visual morbidity in three of our patients. Enlarged blind spot, which has been reported to occur in virtually all eyes with papilledema,was found in our patients also. Accurate visual field testing in children is sometimes difficult to perform, and hence difficult to rely on as the only accurate test. We suggest performing a kinetic perimetry in young and uncooperative children. Symmetric papilledema was recorded in eighteen children and one boy had unilateral papilledema.In this series, all our patients were referred to neurophysician and medically managed with oral acetozolamide and responded well to treatment. None of our patients needed Optic nerve sheath decompression.

Brain tumors with the greatest direct threat to the visual pathways are tumors that involve the optic pathway, parasellar tumors, and cerebral hemispheric tumors [8].We had one patient with pilocytic astrocytoma, the commonest cerebral hemispheric lesion which causes vision loss due to secondary optic atrophy following papilledema. Craniopharyngioma, the most common supratentorial tumor of childhood exhibits a bimodal age distribution. In our series, it was diagnosed in a 15-year-old boy with chronic visual deficit in one eye with papilledema [9].Though tuberculosis is common in India, tuberculous brain abscess is rare [10].Our patient with multiple tubercular cerebral abscess and midline shift had papilledema as the primary manifestation and was treated with anti-tuberculous therapy and recovered completely.

In summary, IIH is a common cause of papilledema in Indian children, and they are mostly symptomatic during presentation and respond well to medical management. Prompt diagnosis and proper management can prevent needless blindness resulting from secondary optic atrophy and also play a significant role in saving the life of children. This study emphasizes that ophthalmologists play a key role in monitoring for visual morbidity following papilledema and also stresses upon the interdisciplinary approach for prompt diagnosis and treatment of papilledema.

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Noonan Syndrome in Thai Children

This study describes clinical features of Noonan syndrome and gene mutations, including *PTPN11, SOS1*, and *BRAF* in the Thai population.Widely spaced eyes were the most common finding from the digital facial analysis technology used in this study.

Keywords: *Facial analysis technology, Gene mutation, PTPN11*.

Noonan syndrome is a genetic disorder with an estimated prevalence of 1 in 1,000 to 2,500 live births [1]. The typical facial features include ptosis, widely spaced eyes, down slanted palpebral fissures, and low set ears [2]. Early and accurate diagnosis of NS is essential as each patient needs an individual treatment regimen, and has distinct recurrent risk and prognosis [3]. Due to limited resources for genetic testing for the disorder, facial analysis technology may be useful to identify new cases. The digital facial analysis technology has previously been used to identify individuals with Noonan syndrome from 20

countries. The sensitivity and specificity of the test for Noonan syndrome in the Asian population was reported to be 0.95 and 0.90, respectively [5]. This study reports common physical findings with the facial analysis technology evaluation and genetic testing in children with Noonan syndrome in Thailand.

Participants were enrolled at Chiang Mai University Hospital including patients with clinical features of Noonan syndrome, and those without these features as controls. Informed consent was obtained from all participants. Medical records were also reviewed, and photographs of patients were sent to the Children's National Hospital for analysis *via* secure encrypted email.

Participants were 12 children (4 females) with clinical features of Noonan syndrome. The mean (SD) age was 5.19 (4.53) year (range 3 month – 17 year). Nine children were further evaluated by the digital facial analysis technology (Case No.1-9) and 7 cases (Case No.1-4 and 10-12) were identified by gene sequencing. The details of 12 individuals are shown in ***Web Table* I**.

Hypertrophic cardiomyopathy (HCM) was the most common cardiac defect found in this study, followed by pulmonary valve stenosis (PVS) and atrial septal defect (ASD). Novel gene mutations were found in 57.1% cases with gene sequencing identification. Three genes that carried mutations were *PTPN11* (71.4%), *SOS1* (14.3%) and *BRAF* (14.3%).

The most common phenotype from the digital facial analysis technology in this study is widely spaced eyes, which is consistent with a previous study [5]. Significant different texture features of Thai patients with normal controls were the texture at upper eyelid (P=0.004), nose apex (P<0.001), cupid's bow (P=0.005), oral commissure (P<0.001), center of ala of the nose (P=0.003), and nostril (P<0.001).

The frequency of cardiac defect is different from a previous report from China [6], which found ASD as the most common defect (50%), followed by PVS (20%). Isojima, *et al*. [7] found that PVS was the most common cardiac defect in Japanese patients (52.6%), followed by HCM (27.3%) and ASD (21.4%) [7]. Despite these variations, the three common defects in Noonan syndrome are HCM, PVS, and ASD [8].

Most patients had *PTPN11* gene mutation, similar to the study by Tartaglia, *et al*. [9]. De novo mutations account for 57.1% of cases, consistent with a previous study, which found 60% of cases with novel mutations [10].

As identification was done by clinical features, only severe phenotypes were included in the evaluation by the facial analysis technology or gene testing. Lastly, complete genetic testing for all cases with the facial analysis technology would provide more information adding to the clinical features.

This study describes clinical features of Noonan syndrome and gene mutations in the Thai population. The feature of widely spaced eyes was the most common facial appearance found by digital facial analysis technology. This may be a helpful clue in suspecting Noonan syndrome by clinicians.

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