This study describes clinical features of Noonan syndrome and Noonan Syndrome in Thai Children

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

**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 digital facial analysis technology used in this study.

**Keywords:** Facial analysis technology, Gene mutation, PTPN11.
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 1.

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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