

INTISARI

Latar belakang: *Congenital Talipes Equinovarus* (CTEV) atau *clubfoot* adalah kelainan bawaan pada anak yang belum diketahui secara pasti penyebabnya (*idiopathic*), namun diperkirakan adalah faktor genetik. *Idiopathic* CTEV dapat bersifat *recurrent* maupun *non-recurrent*. Sampai saat ini, belum ada penelitian yang mengeksplorasi profil miRNA sebagai regulator ekspresi gen dan sebagai biomarker *recurrent* maupun *non-recurrent idiopathic* CTEV dengan sampel biologik orang Indonesia.

Tujuan: Menganalisis ekspresi miRNA dan mencari target gen terpengaruh yang berpotensi menjadi penyebab *idiopathic* CTEV, serta faktor epigenetik (lingkungan dan gaya hidup) yang berperan dalam deformitas *varus recurrent idiopathic* CTEV di Indonesia.

Metode penelitian: Studi *cross sectional* ini melibatkan 12 balita laki-laki berusia 2–2.5 tahun yang dibagi menjadi tiga kelompok yaitu *recurrent idiopathic* CTEV, *non-recurrent idiopathic* CTEV, dan kontrol. Analisis profil miRNA (*discovery phase*) dilakukan dengan NanoString nCounter untuk mengidentifikasi miRNA terkait, dilanjutkan dengan validasi menggunakan qRT-PCR.

Hasil: Pada kelompok *recurrent idiopathic* CTEV vs *non-recurrent idiopathic* CTEV didapatkan 1 miRNA *upregulated* yaitu miR-423-5p dan 28 *downregulated*. kelompok *non-recurrent idiopathic* CTEV vs kontrol didapatkan 58 *upregulated* dan 2 *downregulated* yaitu miR-26a-5p dan miR-548d-5p. Kelompok *recurrent idiopathic* CTEV vs kontrol didapatkan 34 *upregulated* dan satu *downregulated* yaitu miR-299-3p. Kelompok *idiopathic* CTEV vs kontrol didapatkan 96 *upregulated* dan satu *downregulated* yaitu miR-26a-5p. Hasil qRT-PCR, pada *recurrent idiopathic* CTEV, didapatkan peningkatan ekspresi miR-423-5p jika dibandingkan dengan *non-recurrent idiopathic* CTEV maupun kontrol. Pada *recurrent* dan *non-recurrent idiopathic* CTEV didapatkan peningkatan ekspresi miR-584-5p dibandingkan dengan kontrol. Gen yang terpengaruh adalah ZZZ3 dan IGF1R, di mana berdasarkan hasil qRT-PCR dan elektroforesis kedua gen ini mengalami supresi.

Simpulan: miR-584-5p berpotensi menjadi *biomarker idiopathic* CTEV, sedangkan miR-423-5p berpotensi menjadi *biomarker* rekurensi *idiopathic* CTEV.

Kata kunci: *Idiopathic* CTEV, *recurrent*, miRNA, epigenetik, nanostring

ABSTRACT

Background: *Congenital Talipes Equinovarus (CTEV), or clubfoot, is a congenital deformity in children with an unknown definitive cause (idiopathic), although it is suspected to be influenced by genetic factors. Idiopathic CTEV can be either recurrent or non-recurrent. To date, no studies have explored the miRNA profile as a regulator of gene expression and as a biomarker for recurrent and non-recurrent idiopathic CTEV using biological samples from the Indonesian population.*

Objective: *To analyze miRNA expression and identify the affected target genes that may potentially cause idiopathic CTEV, as well as to investigate epigenetic factors (environmental and lifestyle) that contribute to the varus deformity in recurrent idiopathic CTEV in Indonesia.*

Research method: *This cross-sectional study involved 12 male toddlers aged 2–2.5 years, divided into three groups: recurrent idiopathic CTEV, non-recurrent idiopathic CTEV, and controls. miRNA profiling (discovery phase) was conducted using the NanoString nCounter to identify relevant miRNAs, followed by validation using qRT-PCR.*

Results: *In the comparison between the recurrent idiopathic CTEV and non-recurrent idiopathic CTEV groups, one upregulated miRNA was identified (miR-423-5p), along with 28 downregulated miRNAs. In the non-recurrent idiopathic CTEV vs control group, 58 miRNAs were upregulated and 2 were downregulated (miR-26a-5p and miR-548d-5p). In the recurrent idiopathic CTEV vs control group, 34 miRNAs were upregulated and one was downregulated (miR-299-3p). In the combined idiopathic CTEV vs control group, 96 miRNAs were upregulated and one miRNA (miR-26a-5p) was downregulated. qRT-PCR results showed increased expression of miR-423-5p in recurrent idiopathic CTEV compared to both non-recurrent idiopathic CTEV and control groups. Additionally, both recurrent and non-recurrent idiopathic CTEV groups showed elevated expression of miR-584-5p compared to controls. The affected genes were ZZZ3 and IGF1R, both of which were found to be suppressed based on qRT-PCR and electrophoresis results.*

Conclusion: *miR-584-5p has the potential to serve as a biomarker for idiopathic CTEV, while miR-423-5p may serve as a potential biomarker for recurrent idiopathic CTEV.*

Keywords: *Idiopathic CTEV, recurrent, miRNA, epigenetics, nanostring.*