

Abstrak

Latar belakang : Hipertensi arteri pulmonal (HAP) merupakan penyakit progresif dengan prognosis yang buruk dan tingkat mortalitas tinggi, serta membutuhkan pemeriksaan invasif untuk penegakkan diagnosis. *Circular RNA (circRNA)*, sebagai molekul non koding dengan struktur melingkar yang stabil dan spesifik terhadap jaringan, memiliki potensi sebagai biomarker noninvasif melalui pendekatan *liquid biopsy*.

Tujuan: Mengidentifikasi potensi *circRNA* sebagai biomarka diagnostik noninvasif untuk hipertensi arteri pulmonal pada pasien defek septum atrium dewasa (HAP-DSA) yang belum dikoreksi di RSUP Dr. Sardjito Yogyakarta.

Metode: Penelitian dilakukan menggunakan pendekatan profiling dengan mikroarray, validasi ekspresi menggunakan *qRT-PCR*, dan identifikasi fungsi biologis kandidat *circRNA* secara bioinformatik.

Hasil: Profil ekspresi *circRNA* menunjukkan perbedaan yang bermakna antara kelompok HAP-DSA dan kontrol (DSA-non HP), dengan 26 *circRNA* mengalami upregulasi dan 30 *circRNA* mengalami downregulasi. Salah satu *circRNA*, *hsa_circ_0086475* (mengalami downregulasi), diidentifikasi sebagai kandidat biomarker utama berdasarkan analisis ekspresi dan relevansi biologisnya. Ekspresi *hsa_circ_0086475* menunjukkan hubungan yang signifikan ($p < 0,05$) terhadap *mPAP* dan *PVRI* pada subjek perempuan, namun tidak ditemukan hubungan serupa pada subjek laki-laki. Analisis bioinformatik lebih lanjut menunjukkan keterlibatan *hsa_circ_0086475* dalam meregulasi gen-gen kunci yang berperan dalam patogenesis HAP, seperti *BMPR2*, *ATP13A3*, *CAV1*, dan *GDF2*.

Simpulan: Berdasarkan ekspresi dan fungsi biologisnya *hsa_circ_0086475* memiliki potensi sebagai biomarker diagnostik noninvasif terhadap HAP-DSA.

Kata kunci: *Biomarker, circular RNA, congenital heart disease, pulmonary arterial hypertension*

Abstract

Background: *Pulmonary arterial hypertension (PAH) is a progressive disease with poor prognosis and high mortality, often requiring invasive procedures for diagnosis. Circular RNAs (circRNAs), non-coding RNAs with a stable circular structure and high tissue specificity, have emerged as promising noninvasive biomarkers through liquid biopsy approaches.*

Objective: *To identify the potency of circRNAs as noninvasive diagnostic biomarkers for PAH in adult patients with uncorrected atrial septal defect (PAH-ASD) at Dr. Sardjito General Hospital, Yogyakarta.*

Methods: *This study employed microarray-based circRNA profiling, expression validation through qRT-PCR, and identification of circRNA biological function based on bioinformatic analysis.*

Results: *The circRNA expression profile showed significant differences between the PAH-ASD and control (ASD-non-PH) groups, with 26 circRNAs upregulated and 30 circRNAs downregulated. One circRNA, hsa_circ_0086475 (downregulated), was identified as a key biomarker candidate based on expression analysis and its biological relevance. The expression of hsa_circ_0086475 showed a significant association ($p < 0.05$) with mPAP and PVRI in female subjects, but no similar association was found in male subjects. Further bioinformatic analysis showed the involvement of hsa_circ_0086475 in regulating key genes involved in the pathogenesis of PAH, such as BMPR2, ATP13A3, CAV1, and GDF2.*

Conclusion: *Based on their expression profiles and biological functions, hsa_circ_0086475 demonstrate potency as noninvasive diagnostic biomarkers for PAH-ASD.*

Keywords: *Biomarker, circular RNA, congenital heart disease, pulmonary arterial hypertension*