

INTISARI

Latar Belakang: Asma merupakan penyakit inflamasi kronik saluran napas pada anak yang dipengaruhi oleh interaksi faktor genetik dan lingkungan. Polimorfisme *ADAM33* (rs2280091) berperan dalam proses remodeling saluran napas, sedangkan *ORMDL3* (rs12603332) terlibat dalam regulasi respons imun jalur Th2. Meskipun asosiasi kedua varian genetik ini telah dilaporkan pada berbagai populasi, data pada anak Indonesia masih sangat terbatas, sehingga penelitian ini penting untuk mengklarifikasi peran predisposisi genetik dalam patogenesis asma pada populasi anak di Indonesia.

Tujuan: Penelitian ini bertujuan untuk menganalisis hubungan antara polimorfisme rs2280091 gen *ADAM33* dan rs12603332 gen *ORMDL3* dengan kejadian asma pada anak, serta mengevaluasi distribusi frekuensi genotipe dan alel dari kedua polimorfisme tersebut

Metode: Penelitian observasional analitik dengan desain kasus-kontrol melibatkan 76 subjek (38 anak asma dan 38 kontrol sehat) usia 6–18 tahun. Deteksi polimorfisme dilakukan menggunakan metode *Polymerase Chain Reaction–Restriction Fragment Length Polymorphism* (PCR-RFLP). Analisis statistik menggunakan uji chi-square dan regresi logistik untuk menghitung *Odds Ratio* (OR) dengan interval kepercayaan 95%.

Hasil: Polimorfisme rs2280091 *ADAM33* ditemukan pada 44,7% kelompok asma dan 18,4% kelompok kontrol ($p=0,026$; $OR=3,58$; $CI_{95\%}: 1,267–10,143$). Polimorfisme rs12603332 *ORMDL3* ditemukan pada 76,3% kelompok asma dan 39,5% kelompok kontrol ($p=0,003$; $OR=4,94$; $CI_{95\%}: 1,834–13,312$). Frekuensi genotipe AG dan alel G pada polimorfisme rs2280091 gen *ADAM33* serta genotipe CC dan alel C pada polimorfisme rs12603332 gen *ORMDL3* (CC) lebih sering ditemukan pada kelompok anak dengan asma dibandingkan kelompok kontrol. Analisis multivariat menunjukkan bahwa polimorfisme *ORMDL3* merupakan faktor risiko independen yang paling dominan terhadap kejadian asma pada anak.

Kesimpulan: Terdapat hubungan yang bermakna antara polimorfisme rs2280091 *ADAM33* dan rs12603332 *ORMDL3* dengan kejadian asma pada anak dengan peningkatan risiko masing-masing sebesar 3,6 kali dan 5 kali. Hasil penelitian ini mendukung peran predisposisi genetik dalam patogenesis asma pada anak Indonesia.

Kata kunci: asma anak, *ADAM33*, *ORMDL3*, polimorfisme genetik, PCR-RFLP, faktor risiko genetik

ABSTRACT

Background: Asthma is a chronic inflammatory airway disorder in children resulting from complex interactions between genetic susceptibility and environmental exposures. The *ADAM33* rs2280091 polymorphism has been associated with airway remodeling, while the *ORMDL3* rs12603332 variant plays a role in Th2-mediated immune regulation. Although these genetic variants have been linked to asthma in multiple ethnic populations, evidence in Indonesian children remains scarce. Clarifying their contribution within this population is therefore essential to better understand genetic predisposition to childhood asthma.

Objective: To investigate the association between *ADAM33* rs2280091 and *ORMDL3* rs12603332 polymorphisms and childhood asthma, and to determine the genotype and allele frequency distributions of these variants.

Methods: A case-control study was conducted involving 76 subjects (38 children with asthma and 38 age- and sex-matched healthy controls) aged 6–18 years. Genotyping was performed using polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP). Associations were analyzed using chi-square tests and multivariate logistic regression to estimate odds ratios (ORs) with 95% confidence intervals (CIs).

Results: The *ADAM33* rs2280091 polymorphism was present in 44.7% of asthmatic children compared to 18.4% of controls ($p=0.026$; OR=3.58; 95% CI: 1.27–10.14). The *ORMDL3* rs12603332 polymorphism was detected in 76.3% of cases and 39.5% of controls ($p=0.003$; OR=4.94; 95% CI: 1.83–13.31). The AG genotype and G allele of the *ADAM33* rs2280091 polymorphism, along with the CC genotype and C allele of the *ORMDL3* rs12603332 polymorphism, were more frequently observed in children with asthma than in controls. Multivariate analysis identified the *ORMDL3* variant as the strongest independent genetic risk factor for childhood asthma.

Conclusion: Both *ADAM33* rs2280091 and *ORMDL3* rs12603332 polymorphisms are significantly associated with childhood asthma, conferring approximately 3.6-fold and 5-fold increased risks, respectively. These findings reinforce the contribution of genetic susceptibility to asthma pathogenesis among Indonesian children.

Keywords: childhood asthma, *ADAM33*, *ORMDL3*, genetic polymorphism, PCR-RFLP, genetic susceptibility