**Objectives**: Invasive aspergillosis (IA) is the most common invasive fungal infection caused by filamentous fungi in pediatric patients with risk factors. Recently, an increase in cases of azole-resistant (azole-R) IA in adults has been reported. Objective: To describe six pediatric cases of azole-R IA in Spain.

**Materials & Methods:** Descriptive retrospective study, including patients ≤18 years old with probable/proven azole-R IA between 2019 and 2024 in three Spanish tertiary hospitals.

**Results**: Six cases of Azole-R IA are reported (3 proven/3 probable), representing 12.5% (6/48) of all AI during the study period. Median age was 14.5 years (IQR 7-17) with equal gender distribution. All had risk factors: 4 hematological pathology (2 HSCT, 1 AML, 1 ALL-B) and 2 cardiac transplant. Most (5/6) developed breakthrough AI; prior prophylaxis was posaconazole (3 patients: 2 tablets, 1 oral suspension with plasma concentrations within therapeutic range) and liposomal amphotericin B (2 patients). All patients presented pulmonary IA, with compatible radiological findings, although variable among patients. The most frequently isolated species was A*spergillus fumigatus* (5/6), 4 identified as *A. fumigatus sensu stricto.* Although the diagnosis of resistance was relatively late (median: 17 days, IQR 9-25.8), all patients received at least partially active antifungal from diagnosis. Definitive treatment was based on liposomal amphotericin B, combined in 4 cases with an echinocandin. Despite multimodal treatment, the attributable mortality to IA was high (4/6 patients).

**Conclusions**: Azole-R IA should be considered in pediatric patients presenting breakthrough AI having received prior azole prophylaxis, particularly in case of adverse disease progression. Performing invasive tests, identifying the species and resistances, are fundamental to optimize their treatment. In case of IFI under azoles prophylaxis, an antifungal from another family should be added or switched.