AZOLE AND AMPHOTERICIN B RESİSTANT *ASPERGILLUS FUMIGATUS* STRAINS ISOLATED FROM CLINICAL SPECIMENS AND ENVIRONMENT IN AZERBAIJAN.

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PURPOSE

Aspergillus fumigatus is ubiquitous saprophytic mold associated with variety of pathological conditions in human. Small diameter of conidia facilitates their passage to low respiratory tract airways making *A. fumigatus* the commonest etiological agent of aspergillosis. Azoles act on enzyme 14α-demethylase coded by cyp51 gene and block synthesis of ergosterol – the fungal cell wall component. It results in accumulation of toxic methylated sterols in cell and its damage.

•Recently, intensive use of azoles in treatment and agriculture has resulted in emergence of azole-resistant strains. The aim of current investigation was to evaluate prevalence of azole resistant *A.fumigatus* strains in environment and clinical samples of patients applied to hospitals of Azerbaijan Republic.

METHODS

Both clinical and environmental samples were gathered during 2017-2019 period. Environmental samples were collected from 8 regions of Azerbaijan Republic. Clinical specimens were collected from patients applied to Scientific-Research Clinical Microbiological Laboratory, Educational-Therapeutic clinic of Azerbaijan Medical University and Scientific Research Institute of Lung Diseases of Azerbaijan Republic. Identification of strains was performed on basis of cultural, morphological features with subsequent molecular genetic analysis of internal transcribing spacer regions 1 and 4 (ITS1 and ITS4). All strains were tested for susceptibility to voriconazole (VOR), posaconazole (POS) and amphotericin B (AMB) in accordance to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.

RESULTS

44 *A.fumigatus* strains of clinical and environmental origin were isolated and identified. Results of antifungal susceptibility of these strains are represented in table 1. Among 44 isolates 3 were resistant to both azoles, 38 – to POS, 20 – to AMB. Among 34 environmental isolates 27 were resistant to POS, 14 – to AMB. 6 POS resistant strains were also resistant to AMB. 1 isolate was resistant to both azoles and was isolated from public garden in southern part of Azerbaijan Republic. 9 strains out of 10 clinical isolates were resistant to POS, 2 of which were also resistant to VOR. 3 strains were resistant to POS and AMB.

Source (n)	Antifungal agent	MIC (mg/l)							
		≤0.12	0.25	0.5	1	2	4	8	≥16
Clinical isolates (10)	VOR	-	1	4	1	2	2	-	-
	POS	-	1	1	8	-	-	-	-
	AMB	-	-	-	2	5	3	-	-
Environmental isolates (34)	VOR	-	11	14	7	1	1	-	-
	POS	3	4	18	8	1			-
	AMB	-	-	-	7	12	11	1	3

Table 1. Antifungal susceptibility of 44 *A.fumigatus* strains to 3 antifungal drugs.

The results of investigation have shown high overall prevalence of azole resisant *A.fumigatus* isolates in the environment (12.2%) and unexpectedly high resistance rate (90%) in clinical samples. The main reason for this high resistance rate in clinical strains is low number (10 strains) of investigated isolates. Taking into account high environmental prevalence of resistant strains and possible linkage between clinical and environmental isolate we consider that resistance rate in clinical samples is high in Azerbaijan Republic.

CONCLUSION

We revealed high resistance rates both in environmental and clinical isolates. Thus, studies should be continued in higher number of clinical strains with subsequent genetic analysis in order to obtain information about genes responsible for resistance and phylogenetic relevance between environmental and clinical strains.

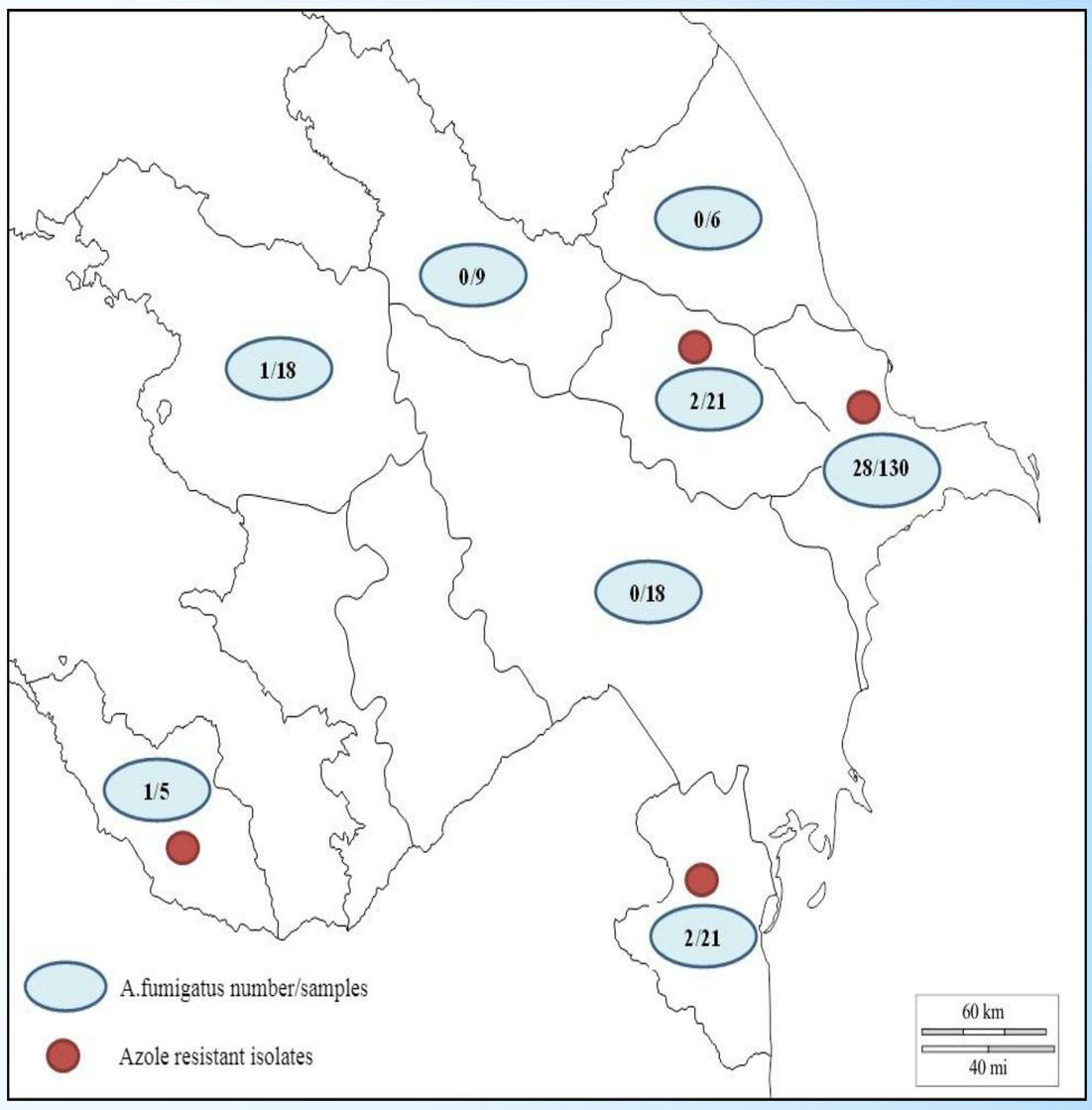

Figure 1. Distribution of 34 environmental A.fumigatus isolates obtained from soil (n=224) and air (n=4) samples in 8 regions of Azerbaijan Republic. Blue circles: *A.fumigatus* number/samples investigated. Red circles: areas with azole resistant strains detected.