

“Expression profile of immunological panel IL1 β , IL10, IL18, TNF- α , TLR4, GATA3, CD68 on cervical samples with positive/negative hr-HPV DNA/E6 E7 mRNA status and cytological estimation.”

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Aim: To investigate IL1 β , IL10, IL18, TNF- α , TLR4, GATA3, CD68 on hr-HPV DNA/hr-HPV E6 E7 mRNA positive/ negative cervical status and LBC estimation

Methods:

- **Clinical control group: (n=40) cervical samples with normal cytology (PAPI/II) and hr-HPV DNA positive status** ➤ **DNA extraction, Real-time qPCR, PCR-based hybridization, cytological examination and photo-documentation techniques were applied.**
- **Clinical group (n=50) with (ASCUS, LSIL, HSIL, CIS, CIN1, CIN2/3+ and more advanced findings) and hr-HPV DNA+.**

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WORKING TO ELIMINATE
LOWER GENITAL TRACT CANCERS

VIROLOGICAL RESULTS: hr HPV DNA (16, 18, 31, 35, 33, 45, 51, 59, 39, 58, 56, 52, 66, 68)

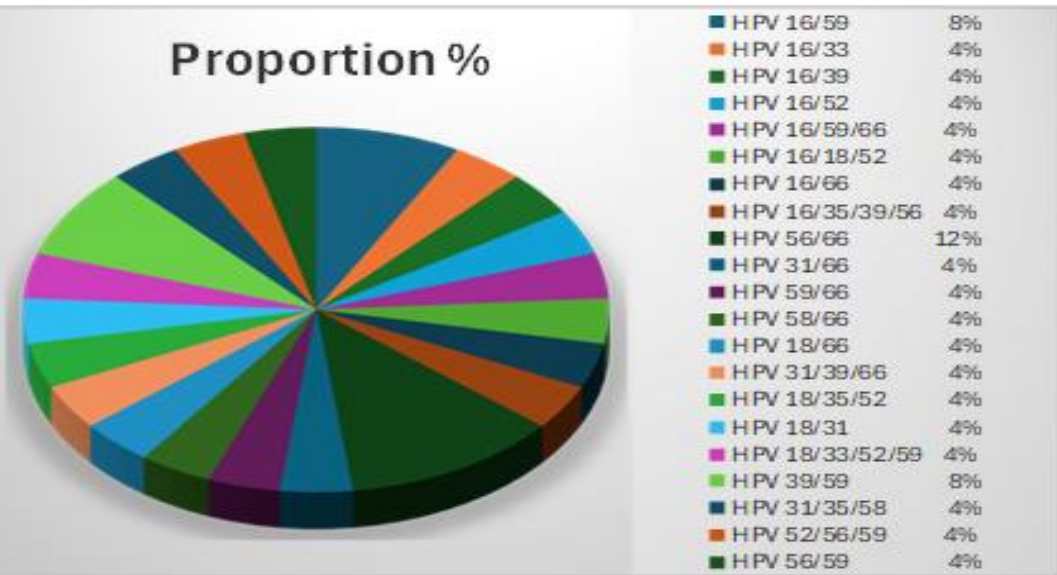
➤ **Type-specific hrHPV frequency in the clinical control group with normal cytology and hrHPV DNA +.**

HPV 16	HPV 18	HPV 31	HPV 33	HPV 35	HPV 39	HPV 45	HPV 51	HPV 52	HPV 56	HPV 58	HPV 59	HPV 66	HPV 68
27%	9%	15%	6%	7%	8%	5%	-	9%	7%	3%	14%	25%	-

➤ **Distribution of co-infectious variants (25%) in the clinical control group with normal cytology, hrHPV DNA+**

- **HPV 16 and HPV 66 were determined to be categorically dominant as a rate of frequency of hrHPV, as well as dominant participants in co-infectious variants, followed by HPV 59, followed by 18 and 31, etc.**

- **36% of co-infectious variants carry HPV 16**
 - **40% % carry HPV 66**



VIROLOGICAL RESULTS: hr HPV DNA (16, 18, 31, 35, 33, 45, 51, 59, 39, 58, 56, 52, 66, 68)

➤ **hrHPV frequency in the clinical group (ASCUS, LSIL, HSIL, CIS, CIN1, CIN2/3+) and hrHPV DNA +.**

HPV 16	HPV 18	HPV 31	HPV 33	HPV 35	HPV 39	HPV 45	HPV 51	HPV 52	HPV 56	HPV 58	HPV 59	HPV 66	HPV 68
66%	6,66%	<u>20%</u>	13,33%	-	-	6,66%	-	<u>20%</u>	6,66%	<u>20%</u>	6,66%	33,3%	-

➤ **Distribution of co-infectious variants (53,33 %) in the clinical group with (ASCUS, LSIL, HSIL, CIS, CIN1, CIN2/3+) and hrHPV DNA +.**

- **equal shares of infectious variants detected of 12.5%.**

- **HPV 16 was determined as dominant in the hrHPV co-infectious variants**

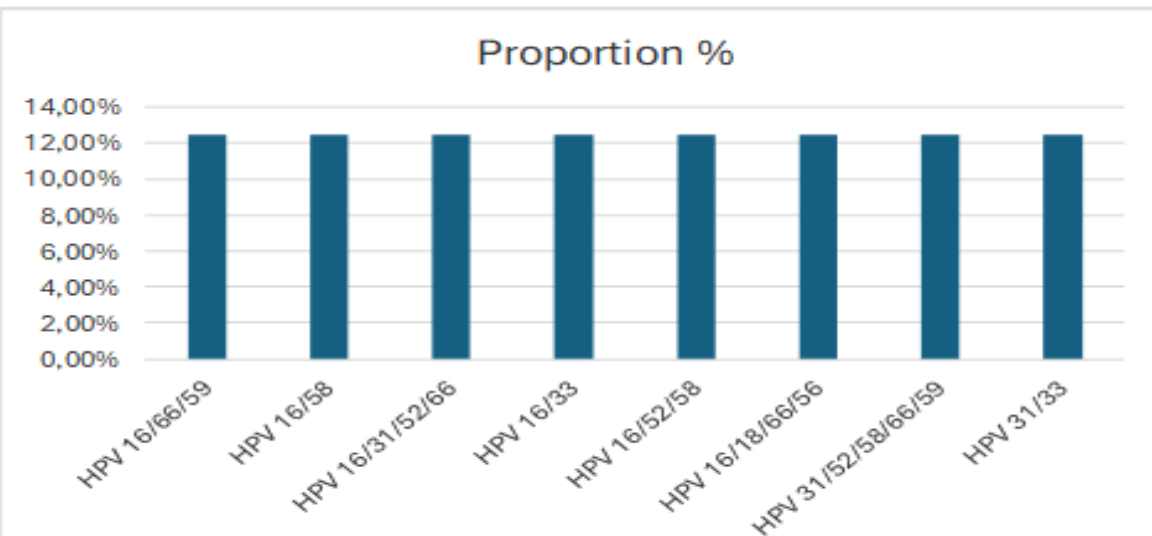
- **75% of the co-infectious variants contain HPV 16.**

- **50% of the co-infectious variants contain HPV 66.**

37.5% of the co-infectious variants contain HPV 58, 52 and 31



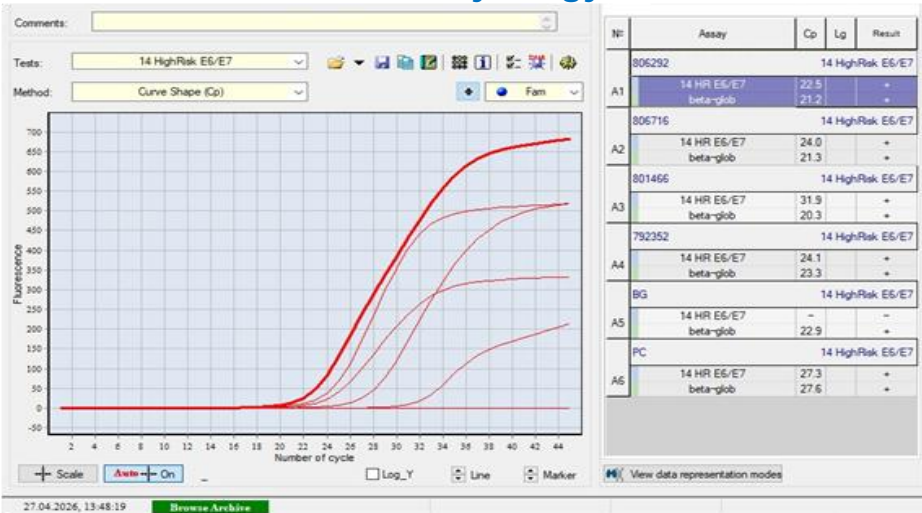
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VIROLOGICAL RESULTS: hr HPV onco E6/E7 mRNA (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)

- 100% of patients were hr-HPV E6/E7 mRNA positive in the clinical hrHPV DNA+ group (ASCUS, LSIL, HSIL, CIS, CIN1, CIN2/3+).

- 58,9% of patients were hr-HPV E6/E7 mRNA positive in the control hrHPV DNA + group with normal cytology.



Real Time PCR results of positive/negative Hr-HPV-E6/E7 mRNA status in Bulgarian patients.

IMMUNOLOGICAL RESULTS (IL1 β , IL10, IL18, TNF- α , TLR4, GATA3, CD68)

- In hr-HPV DNA+ clinical group with abnormal cytology, elevated IFI > 95–100% was found in 95% without reactive cellular changes.
- In hr-HPV DNA + control group /normal cytology, elevated inflammation index (IFI \geq 50) was found in 77.2 % with reactive inflammatory changes and > 50% polymicrobial infection /dysbiosis/.

1	Name of research	Results	Unit	Interpretation	Interval
Evaluation of vaginal local inflammation by method of reverse transcription followed by real-time PCR					
1	IL1B	1.9	Lg		
2	IL10	0.0	Lg		
3	IL18	1.6	Lg		
4	TNFA	1.9	Lg		
5	TLR4	0.0	Lg		
6	GATA3	1.4	Lg		
7	CD68	1.0	Lg		
8	B2M	5.6	Lg	valid	>> 3
9	TLR4/GATA3	0.0	relative units	<-x-]	<< 0.070]
10	TNFA/IL18	2.5	relative units	<-]-x	<< 0.050]
11	IL10/IL18	0.0	relative units	<-x-]	<< 4.0]
12	IL1B/CD68	7.0	relative units	<-x]	<< 12.7]
13	Inflammation index	80.8	%	INFLAMMATORY	< 50

Conclusion:

The expression profile is characteristic for local inflammation.

Elevated IFI = 80.8 % in a studied patient

CONCLUSIONS

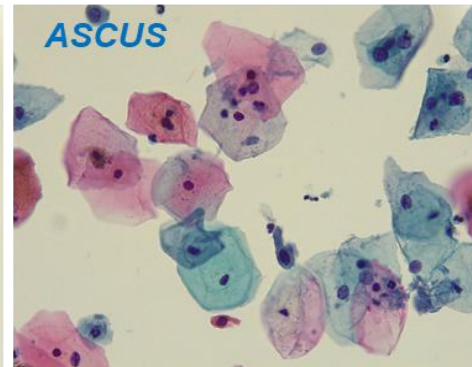
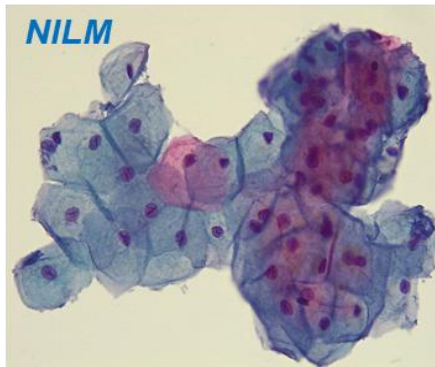
- *IL-1 β , IL-18, TNF- α , and CD68 expression was significantly increased in clinical/ clinical control groups, suggesting also their potential **pro-tumor activity** in addition to pro-inflammatory.*

- *In >50% of studied cases in control group was found predominantly an abundant superficial cervical layer. /10% was secondary established with more advanced cytological findings **HSIL, CIN1, etc./***

- *58.9% of hr-HPV E6/E7 mRNA positive patients in the control group with normal cytology are at a likely higher risk of cervical cancer, despite a normal cytology result- /subjective method with a lot of limitations/*

- *FAM19A4/miR124-2 methylation test on this 58, 9% hr-HPV E6/E7 mRNA +/-normal cytology subgroup will be applied.*

-*The pilot unpublished data showed the need of powerful biomarkers for a reliable stratification of woman in a real higher risk of developing CC.*



Find them even before they appear or when they are "invisible" !!!