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High-risk Human Papillomavirus (hrHPV) Genotypes and Cervical Cancer

Aims & Objectives:

To determine the correlation between HPV subtypes *16, 18 and 'other'* and the histological diagnosis of CGIN & SMILE, SCC and Adenocarcinoma

Background

- pHPV is an automated molecular test introduced as a more sensitive method of detecting cervical lesions and used as first line of investigation
- pHPV test specifically identifies HPV 16 and 18 while concurrently detecting 'other' 12 high risk types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)
- Molecular platform used at RWT : Roche Cobas 6800 and 8800
- Cobas HPV test is based on 2 major processes:
  1. Extraction of HPV and cellular DNA and
  2. PCR amplification of target DNA

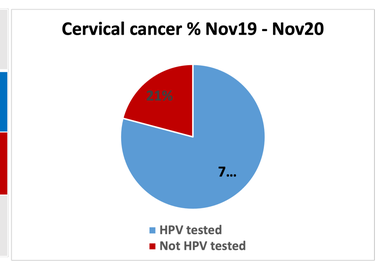
Method

- Data were collected retrospectively from Nov 2019 – Nov 2020 by running colposcopy extraction access database 'Colp database'
- 15 tables set up to extract data for different colposcopy units within the West Midlands
- Two searches set up:
  1. Extracted all cervical cancer cases
  2. Extracted CGIN & SMILE cases.

Results

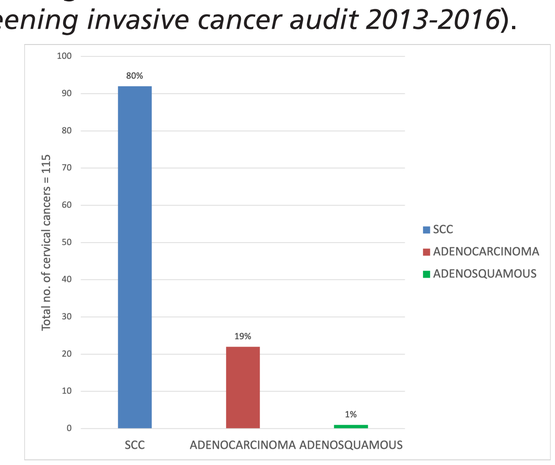
- Cervical cancer cases Nov 2019 – Nov 2020: 115 cases identified
- 21% referred directly to Gynae dept. due to clinical symptoms with no cervical screening intervention
- 79% of cervical cancers identified by cervical screening test: importance and effectiveness of screening programme.

Cervical Cancer Cases Nov 19 – Nov 20		
HPV tested	91	79%
Not HPV tested (Referred due to symptoms)	24	21%
Total	115	100%



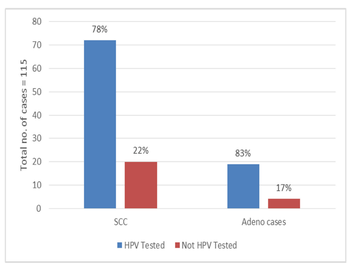
115 cervical cancers:

- 92 (80%) SCC
- 22 (19%)Adenocarcinoma
- 1 case Adenosquamous
- These results are in line with the published cervical screening invasive cancer audit (PHE 2019, *Cervical screening invasive cancer audit 2013-2016*).



HPV tested vs non HPV (clinically) detected cancers

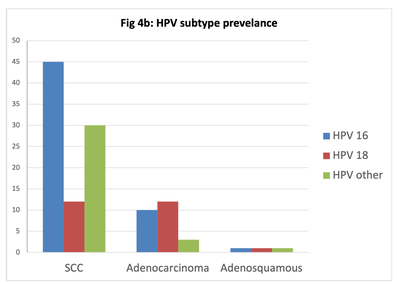
	SCC	%	Adeno cases	%
HPV Tested	72	78%	19	83%
Not HPV Tested	20	22%	4	17%
Total	92	100%	23	100%



HPV Subtype data

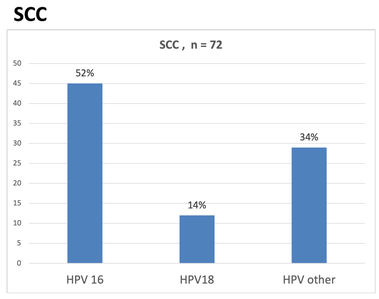
- HPV subtype data were gathered for the entire 91 hr HPV positive cancers.

HPV Subtype	SCC	Adenocarcinoma	Adenosquamous
HPV 16	31 (2 CGIN)	8 (1 CIN)	
HPV 18	10 (3 cases CGIN, 1 SMILE)	8 (1 CIN)	
HPV 'other'	17	0	
HPV 16, 18	1	0	
HPV 16, 18 and 'other'	1 (+ CGIN)	1 (+ CIN)	1
HPV 16 , 'other'	12	0	
HPV 18, 'other'	0	1	
Total	72	18	1

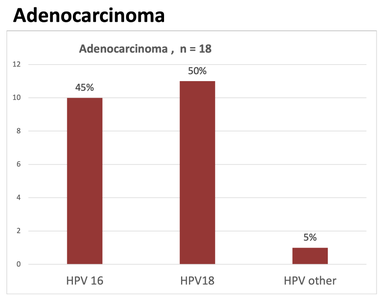


Combined HPV Subtype data (presence of single or multiple HPV subtypes)

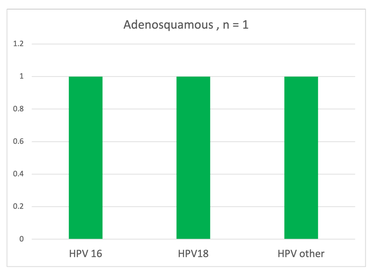
SCC



Adenocarcinoma



Adenosquamous



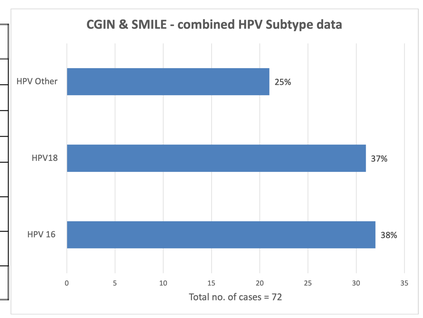
CGIN & SMILE

- 77 CGIN cases were identified for the period of Nov 19 – Nov 2020
- 94% detected by HPV testing compared to 6% detected via referral for clinical symptoms.

CGIN & SMILE cases Nov 2019 – Nov 2020		
HPV tested	72	94%
Not HPV tested	5	6%
Total	77	

CGIN & SMILE: HPV subtype data

HPV Subtype	CGIN Cases & SMILE	%
HPV 16	29	40%
HPV 18	22	31%
HPV 'other'	10	14%
HPV 16, 18	0	0%
HPV 16, 18 and 'other'	1	1%
HPV 16 , 'other'	2	3%
HPV 18, 'other'	8	11%
Total	72	100%



Discussion

1. HPV 16 is the most prevalent subtype in SCC cases followed by HPV 'other' and then HPV 18. This is an unusual finding with regards to emergence of HPV subtype 'other' in SCC cases compared to previous studies (Ayatollahi, H. et al. 2014) which showed prevalence of HPV 16, followed by HPV 18 and then HPV 'other' n SCC cases.
2. Adenocarcinoma and CGIN cases shows that HPV 18 and 16 were closely associated HPV subtypes compared to previously published studies (Clifford et al. 2003) which showed HPV 18 as the most prevalent subtype in glandular lesions.

The possible explanation for the above-mentioned variations in our audit could be because of geographical area, age and effects of vaccination on this cohort of patients. Further information on prevalence of 'other' HPV subtypes will depend on availability of suitable assay kits from manufacturers.

The data on HPV subtype results could provide vital information for the Pharmaceutical companies to modify and create HPV subtype specific vaccinations.

Conclusion

HPV 16 is the most prevalent subtype in SCC cases, followed by HPV 'other' and then HPV 18. Adenocarcinoma and CGIN cases are associated with HPV 18 as the highest proportion and closely followed by HPV 16.

Limitations

Due to time constraints, I was unable to produce data on CIN3 cases to include in this audit, which would have provided useful information regarding HPV subtype correlation between CIN3 and SCC.

The case numbers used for this study might not be a true representation of total number of cancer cases expected per year due to effects of COVID-19 pandemic during this period on women attending for screening and subsequent diagnosis.

Acknowledgments

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References

- Clifford, G., Smith, J., Plummer, M. et al. (2003) Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. Br J Cancer 88, 63–73. https://doi.org/10.1038/sj.bjc.6600688
- Ayatollahi, H., Homaei-Shandiz, F., Kooshyar, M. M., Tabatabaee-Yazdi, S. A., Mehrjerdian, M., Jafarian, A. H., Sadeghian, M. H., Keramati, M. R., Ghasemian-Moghadam, H. R., & Sheikhi, M. (2014). Human papilloma virus 16/18 genotypes in patients with squamous cell carcinoma of cervix in northeast Iran. Nigerian medical journal : journal of the Nigeria Medical Association, 55(6), 495–498. https://doi.org/10.4103/0300-1652.144706 [Date of Access 20th April 2021]
- PHE Publication. (2019) Cervical screening: invasive cervical cancer audit 2013 to 2016. Cervical Screening Programme England. Available from: https://www.gov.uk/government/publications/cervical-screening-invasive-cervical-cancer-audit-2013-to-2016 [Accessed 30th Jan 2021]
- Jihad N.A., Naif M.H. and Sabri E. H. (2020) Prevalence of high risk human papilloma virus among Iraqi women with abnormal cervical cytology, Elsevier. vol 21, 100871 https://doi.org/10.1016/j.genrep.2020.100871 [Date of Access 3rd March 2021]
- Hang, D., Jia, M., Ma, H., Zhou, J., Feng, X., Lyu, Z., Yin, J., Cui, H., Yin, Y., Jin, G., Hu, Z., Shen, H., Zhang, K., Li, N., & Dai, M. (2017). Independent prognostic role of human papillomavirus genotype in cervical cancer. BMC infectious diseases, 17(1), 391. https://doi.org/10.1186/s12879-017-2465-y [Date of Access 3rd March 2021]
- Zampronha, R., Freitas-Junior, R., Murta, E. F., Michelin, M. A., Barbaresco, A. A., Adad, S. J., Oliveira, A. M., Rassi, A. B., & Oton, G. J. (2013). Human papillomavirus types 16 and 18 and the prognosis of patients with stage I cervical cancer. Clinics (Sao Paulo, Brazil), 68(6), 809–814. https://doi.org/10.6061/clinics/2013(06)14 [Date of Access 20th April 2021]
- Chen A.A., Gheit T, Franceschi S, Tommasino M, Clifford GM, (2015) Human papillomavirus 18 genetic variation and cervical cancer risk worldwide. J Virol 89:10680–10687. doi:10.1128/JVI.01747-15. [Date of Access 3rd March 2021]

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