PREVALENCE OF HIV INDICATOR CONDITIONS IN LATE PRESENTING PATIENTS WITH HIV: A MISSED OPPORTUNITY FOR DIAGNOSIS?

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Yi dan Lin, Sarah Garner, Jillian Lau, Tony Korman and Ian Woolley

Disclosure of Interest

None

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Background

- 39 per cent of new HIV diagnoses had a CD4 count of less than 350
- Late diagnosis is associated with increased HIV-related morbidity and mortality and health care costs e.g. hospitalisations
- Significant public health importance
  - 10–20 per cent of Australians living with HIV have not been diagnosed

Department of Health, National HIV Strategy, 2014

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HIV indicator based testing

- Since 2008, European AIDS Clinical Society (EACS) [1]and British HIV association (BHIVA) has recommended for HIV indicator condition based testing.[2] ASHM also recommends this in its testing guidelines.[3]
- Routine testing for conditions with a HIV prevalence > 0.1% has been reported to be cost-effective[1]
- Does not require identification of high risk group by clinician or patient
- Normalises HIV testing and decreases stigma

1. HIV in Europe, accessed at http://hiveurope.eu/Portals/0/Guidance.pdf.pdf, 2012
2. BHIVA, accessed at http://bhiva.org/HIV-testing-guidelines.aspx, 2008
3. ASHM, National HIV Testing Policy 2017

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HIV Indicator diseases across Europe (HIDES I) study

	HIV test	HIV +	Prevalence (95%CI)	
Total	3588	66	1.84	(1.42-2.34)
STI	764	31	4.06	(2.78-5.71)
Malignant lymphoma	344	1	0.29	(0.01-1.61)
Cervical or anal dysplasia	542	2	0.37	(0.04-1.32)
Herpes Zoster <65yo	207	6	2.89	(1.07-6.21)
Hepatitis B/C	1099	4	0.36	(0.10-0.93)
On-going mononucleosis-like illness	441	17	3.85	(2.26-6.10)
Leuko/thrombocytopaenia	94	3	3.19	(0.66-9.04)
Seborrheic dermatitis/exanthema	97	2	2.06	(0.25-7.24)

Sullivan et Al. PLoS ONE, 2013, Volume 8, Issue 1, e52845

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HIDES I Study

- Median CD4 (n=35/66): 400 cells/uL (11-675)
- 11% hospitalized – 71% of those with AIDS or infection
- 20% had potentially HIV-related presentations in the prior years
  - 23% had more than one presentation

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Sullivan et Al. PLoS ONE, January 2013, Volume 8, Issue 1, e52845

1. Conditions which are AIDS defining among PLHIV*

Strongly recommend testing:

Neoplasms:
- Cervical cancer
- Non-Hodgkin lymphoma
- Kaposi's sarcoma

Bacterial infections
- Mycobacterium Tuberculosis, pulmonary or extrapulmunary
- Mycobacterium avium complex (MAC) or Mycobacterium kansasii, disseminated or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated or extrapulmunary
- Pneumonia, recurrent (2 or more episodes in 12 months)
- Salmonella septicaemia, recurrent

Viral infections
- Cytomegalovirus retinitis
- Cytomegalovirus, other (except liver, spleen, glands)
- Herpes simplex, ulcer(s) >1 month/bronchitis/pneumonitis
- Progressive multifocal leucoencephalopathy

Parasitic infections
- Cerebral toxoplasmosis
- Cryptosporidiosis diarrhoea, >1 month
- Isosporiasis, >1 month
- Atypical disseminated leismaniasis
- Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis)

Fungal infections
- Pneumocystis carinii pneumonia
- Candidiasis, oesophageal
- Candidiasis, bronchial/ tracheal/ lungs
- Cryptococcosis, extra-pulmonary
- Histoplasmosis, disseminated/ extra pulmonary
- Coccidiodomycosis, disseminated/ extra pulmonary
- Penicilliosis, disseminated

2a. Conditions associated with an undiagnosed HIV prevalence of >0.1 %**

Strongly recommend testing:

- Sexually transmitted infections
- Malignant lymphoma
- Anal cancer/dysplasia
- Cervical dysplasia
- Herpes zoster
- Hepatitis B or C (acute or chronic)
- Mononucleosis-like illness
- Unexplained leukocytopenia/ thrombocytopenia lasting >4 weeks
- Seborrheic dermatitis/exanthema
- Invasive pneumococcal disease
- Unexplained fever
- Candidaemia
- Visceral leishmaniasis
- Pregnancy (implications for the unborn child)

HIV in Europe, accessed at http://hiveurope.eu/Portals/0/Guidance.pdf.pdf, 2012

2b. Other conditions considered likely to have an undiagnosed HIV prevalence of >0.1%

Offer testing:

- Primary lung cancer
- Lymphocytic meningitis
- Oral hairy leukoplakia
- Severe or atypical psoriasis
- Guillain–Barré syndrome
- Mononeuritis
- Subcortical dementia
- Multiplesclerosis-like disease
- Peripheral neuropathy
- Unexplained weightloss
- Unexplained lymphadenopathy
- Unexplained oral candidiasis
- Unexplained chronic diarrhoea
- Unexplained chronic renal impairment
- Hepatitis A
- Community-acquired pneumonia
- Candidiasis

3. Conditions where not identifying the presence of HIV infection may have significant adverse implications for the individual's clinical management despite that the estimated prevalence of HIV is most likely lower than 0.1%

Offer testing:

- Conditions requiring aggressive immuno-suppressive therapy:
  - Cancer
  - Transplantation
  - Auto-immune disease treated with immunosuppressive therapy
- Primary space occupying lesion of the brain.
- Idiopatic/Thrombotic thrombocytopenic purpura

HIV in Europe, accessed at http://hiveurope.eu/Portals/0/Guidance.pdf.pdf, 2012

Aim

- Prevalence of HIV indicator conditions in late presenting patients with HIV at Monash Health between 2000 and 2014
  - Would this have been a useful strategy to increase HIV diagnoses?

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Method

- Retrospective chart review of late-presenting patients with HIV (CD4 < 350cells/µL) at Monash Health between 2000 and 2014
- Demographical data: age, sex, country of birth, mode of acquisition, CD4 count at diagnosis, opportunistic infection at diagnosis of late-presenters vs rest of HIV cohort
- Descriptive statistics was applied and comparisons were made using chi-square tests
- Assessed for any EACS listed indicator condition in their prior medical record
- Hepatitis serology, FBE, CD4 count and HIV viral load using pathology database
- Excluded age <18 years old and any indicator condition diagnosed overseas (pregnancy, opportunistic infection)
- Definitions
  - Unexplained weight loss > 10% for at least 30 days
  - Diarrhoea > 4 weeks
  - Unexplained fever > 3 weeks
  - Lymphadenopathy > 4 weeks

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Case 1

74 y.o. woman presents with 10 months of diarrhoea

- 6-8 bowel motions a day
- Loss of weight of 22kg in 8 months (31% of total body weight)
- Recurrent oral candidiasis
- Dysphagia/odynophagia on admission
- started on azathioprine and steroids for 'indeterminate colitis' by gastroenterologist

- Admission 4 months prior under gastroenterology:
  - Gastroscopy showed suspected oesophageal candidiasis
  - Colonoscopy showed 'non-specific colitis' – biopsy not suggestive of IBD or malignancy
  - Fevers/night sweats with documented fever 38 degrees celsius
  - CD4 count ordered but not noted: CD4 count 208, CD4 16%

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Case 2

41 man presents with HIV encephalopathy with 3 months of:

- Loss of weight of 14 kg (17% total body weight)
- Fevers and night sweats
- Hepatosplenomegaly
- Lymphadenopathy
- Multiple episodes of mononeuritis presenting in the three years prior
- Anorexia due to candidiasis
- Pancytopenia
  - Hb 116, WCC 3.7, Plt 78 - lymphocytes 0.4
  - Underwent bone marrow biopsy and trephine x2
    - hypercellular bone marrow - "Is there any evidence of a viral infection?"

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Demographics

	Late Presenters (n=82)	Control (n=354)	p-value
Age (years)	45 (9-85)	39 (0-82)	0.05
Sex			0.11
Male	68 (83%)	264 (75)	
Female	14 (17%)	90 (25)	
Born overseas	50 (61%)	207 (58%)	p<0.001
Heterosexual transmission	42 (51%)	109 (31%)	
Average CD4 count at diagnosis			
outpatient	212		
inpatient	58		
Opportunistic infection at admission	41 (50%)		
PJP	17 (21%)		

Garner et al, The International Union against Sexually Transmitted Infections (IUSTI) Conference poster, 2016

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EACS HIV Indicator Conditions	Number (n=80)	%
Opportunistic infections	5	6.3
Prevalence in undiagnosed PLHIV > 0.1%	42	52.5
Condition where non-diagnosis significantly impacts management •	2	2.5
Number of Indicator Conditions		
at least 1	44	55.0
at least 2	29	36.3
at least 3	12	15.0
4 or more	5	6.3
Time between indicator condition to HIV diagnosis		
at least 3 months	34	42.5
at least 12 months	22	27.5
Presence of indicator condition by year of HIV diagnosis		
2000-2007	21	26.3
2008-2014	23	28.8

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HIV indicator conditions	N	%
Unexplained loss of weight	25	31.3
Herpes zoster	8	10
Thrombocytopenia/leukopenia	8	10
Candidiasis (oral or oesophageal)	8	10
Community acquired pneumonia	7	8.8
Fevers/night sweats	6	7.5
Viral hepatitis	6	7.5
Diarrhoea	5	6.3
Lymphadenopathy	4	5
Mononucleosis like illness/seroconversion illness	3	3.8
sexually transmitted infection	3	3.8
psoriasis/seborrhoeic dermatitis	2	2.5
peripheral neuropathy	2	2.5
cervical dysplasia	1	1.3

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Discussion

- Limitations of data
  - Retrospective – recall bias
  - May be an underestimate of prevalence of HIV indicator conditions
    - Only one health system
    - No access to primary care record or overseas medical record
- Next step: educate clinicians and ensure HIV indicator condition guidelines recommend HIV testing
- Stigma and clinician barriers regarding HIV testing
  - HIDES 1 study – time, skills, clinician motivation
  - HIDES 2 Study - offer/test rates 31%-99% vs uptake of testing >95%

Conclusion

A majority of late-presenting patients living with HIV had at least one indicator condition prior to diagnosis in our single centre study

This may be a useful strategy to increase early diagnosis and treatment for these patients

May highlight need for more education regarding HIV indicator conditions and reducing clinician barriers in low-case load GP and specialist clinics

Questions?

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