Lymphoid neoplasms in a South African HIV endemic setting categorised according to the WHO-HAEM5

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Background

Lymphomas are prevalent haematolymphoid tumours in SSA and they are impacted by the HIV epidemic.

To our knowledge, there is no high-quality, clinically validated, prospectively maintained, lymphoma registry in South Africa.

New classification systems:

- WHO-HAEM5
- ICC

Require increasingly sophisticated diagnostics - with limited availability in the local context.

Aims

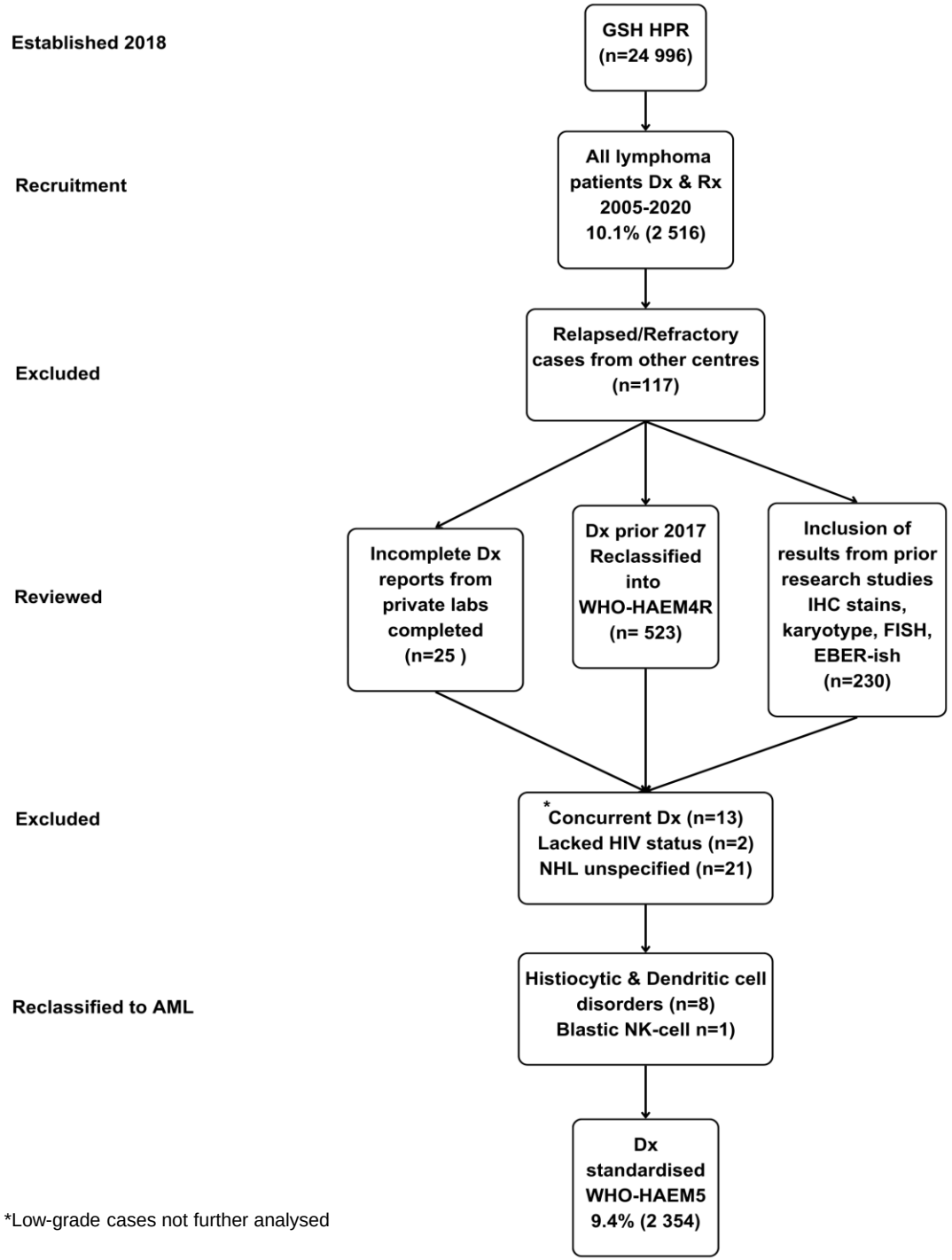
In this study, a robust registry with universally accepted hierarchical taxonomy of lymphoid neoplasms was established (UCT HREC R024/2018)

- to capture and subtype lymphoma

- to generate high quality descriptive real-world data

- alert to trends in high impact varieties

Methods



*Low-grade cases not further analysed

Results

Overall reclassification rate to WHO-HAEM5 25.9% (609)

HIV prevalence 33.1%

EBV prevalence 32.7%

Differences of note between WHO-HAEM5 and ICC:

- tIL 44 (1.9%)
- IDD 957 (40.7%)
- HGBL with *MYC* and *BCL6* rearrangements 1 (0.04%)

Table 1: Baseline characteristics of lymphoma patients diagnosed at GSH between 2005-2020 (WHO-HAEM5)

		Total No. (%)	HIV- (%)	HIV+ (%)
Lymphoma Cohort		2354	1575	779
Sex	Males	1222 (51.9)	822 (52.2)	400 (51.4)
	Females	1132 (48.1)	753 (47.8)	379 (48.7)
Age (years), median (IQR)		47.6 (35.0-62.0)	56.6 (41.0-67.3)	38.3 (32.5-45.3)
Non-Hodgkin lymphoma		1891 (80.3)	1265 (80.3)	626 (80.4)
Tumour-like lesions with B-cell predominance (MCD/IgG4)		77 (3.2)	7 (0.5)	70 (9.0)
Mature B cell				
Pre-neoplastic/neoplastic small lymphocytic proliferations*		203 (8.6)	199 (12.6)	4 (0.5)
Splenic B-cell lymphomas/ leukaemias (HCL/SMZL/SBLPN)		36 (1.5)	36 (2.3)	-
Lymphoplasmacytic lymphoma		20 (0.8)	20 (1.3)	-
Marginal zone lymphoma		66 (2.8)	63 (4.0)	3 (0.4)
Follicular lymphoma		154 (6.5)	153 (9.7)	1 (0.1)
Primary cutaneous follicle centre lymphoma		1 (0.004)	1 (0.1)	-
Mantle cell lymphoma		47 (2.0)	45 (2.9)	2 (0.3)
Transformations of indolent B-cell lymphomas		44 (1.9)	41 (2.6)	3 (0.4)
Diffuse large B-cell lymphoma, *NOS*		588 (25.0)	415 (26.3)	173 (22.2)
T-cell/histiocyte-rich large B-cell lymphoma		17 (0.7)	15 (1.0)	2 (0.3)
EBV-positive DLBCL		49 (2.1)	16 (1.0)	33 (4.2)
Plasmablastic lymphoma		95 (4.0)	7 (0.4)	88 (11.3)
Primary large B-cell lymphoma of immune-privileged sites		24 (1.0)	17 (1.1)	7 (0.9)
Intravascular large B-cell lymphoma		1 (0.004)	1 (0.1)	-
Primary mediastinal large B-cell lymphoma		24 (1.0)	24 (1.5)	-
Mediastinal grey zone lymphoma		3 (0.1)	3 (0.2)	-
High-grade B-cell lymphoma, *NOS*		50 (2.1)	11 (0.7)	39 (5.0)
Burkitt lymphoma		194 (8.2)	23 (1.5)	171 (22.0)
KSHV/HHV8-associated B-cell lymphoid lymphomas (PEL)		6 (0.2)	1 (0.1)	5 (0.6)
Lymphoid proliferations and lymphomas associated with IDD		10 (0.4)	10 (0.7)	-
Mature T/NK cell				
T-cell prolymphocytic leukaemia		5 (0.2)	5 (0.3)	-
T-large granular lymphocytic leukaemia		2 (0.1)	1 (0.1)	1 (0.1)
NK-large granular lymphocytic leukaemia		1 (0.004)	1 (0.1)	-
Adult T-cell lymphoma/leukaemia (HTLV-1-associated)		2 (0.1)	1 (0.1)	1 (0.1)
Mycosis fungoides/ Sezary Syndrome		49 (2.0)	48 (3.1)	1 (0.1)
Primary cutaneous T-cell lymphoid proliferations/ lymphomas		10 (0.4)	9 (0.6)	1 (0.1)
Intestinal T/ NK-cell lymphoid proliferations/lymphomas		1 (0.004)	1 (0.1)	-
Hepatosplenic T-cell lymphoma		5 (0.2)	5 (0.3)	-
Anaplastic large cell lymphoma		39 (1.7)	28 (1.8)	11 (1.4)
Nodal T-follicular helper (TFH) cell lymphoma		13 (0.6)	12 (0.8)	1 (0.1)
EBV-positive NK-cell and T-cell lymphomas		9 (0.3)	6 (0.4)	3 (0.4)
Other peripheral T-cell lymphomas, unspecified		46 (1.9)	40 (2.5)	6 (0.8)
Hodgkin lymphoma		463 (19.7)	310 (19.7)	153 (19.6)
Classic Hodgkin lymphoma		436 (18.5)	284 (18.0)	152 (19.5)
Nodular lymphocyte predominant Hodgkin lymphoma		27 (1.2)	26 (1.7)	1 (0.1)

HIV-related subset

ART status:

-ART naïve [n=334,(42.9%)]

-ART suppressed [n=285, (36.6%)]

-ART unsuppressed [n=160, (20.5%)]

PLWHIV were significantly younger, median 38.3 years (IQR 32.5-45.3) vs HIV-neg patients, median 56.6 years (IQR 41.0-67.3); *P*<0.001.

Most frequent HIV-associated subtypes were:

-DLBCL, *NOS* 22.2%,

-BL 22.0%

-CHL19.5%

-PBL 11.3%

Discussion

Highlights the complexities/challenges to implement updated Dx systems.

Relatively high reclassification rate reflects temporal changes in the multimodal diagnostics of haematological malignancies and in-house operational challenges.

Validates the incorporation of HIV testing into the diagnostic algorithm in HIV endemic regions.

Consolidation of IDD and tIL by WHO-HAEM5 created conceptual groups that generate data conflicts for cancer registries and may require reconsideration in future WHO-HAEM iterations.

Improvement in cost-effective diagnostic & classification algorithms for LMIC.

Supports development of regional specialised cancer registries and research.

Conclusions

By auditing our diagnostic pathway:

- Generated data that validates algorithms tailored to low-resource HIV endemic settings.
- Increased accuracy of downstream subtyping with prospective entries.
- Identified instances of DHL that may have benefitted from FISH.

Future considerations for new classification systems to include HIV testing in diagnostic pathways.

Potential to positively impact patient outcomes by guiding timely and focused treatment planning.

References

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