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Global Oncology

Onkologische Versorgung in Ländern mit niedrigem und mittlerem Einkommen am Beispiel Tansanias

Habilitationsschrift
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Die im Folgenden aufgelisteten sechs Originalarbeiten liegen der kumulativen Habilitationsschrift zugrunde, welche die wesentlichen Ergebnisse der Publikationen zusammenfasst und diskutiert.

1. **Henke O**, Bruchhausen W, Massawe A. (2022). Use of Herbal Medicine Is Associated With Late-Stage Presentation in Tanzanian Patients With Cancer: A Survey to Assess the Utilization of and Reasons for the Use of Herbal Medicine. JCO Glob Oncol 8:e2200069. (IF: 4,325); doi: 10.1200/GO.22.00069.
2. Henke A, Kluge U, Borde T, Mchome B, Serventi F, **Henke O**. (2021). Tanzanian women´s knowledge about Cervical Cancer and HPV and their Prevalence of positive VIA cervical screening results. Data from a Prevention and Awareness Campaign in Northern Tanzania, 2017 – 2019. Glob Health Action 14(1):1852780. (IF: 2,604); doi: 10.1080/16549716.2020.1852780.
3. Singer R, Henke A, Alloyce JP, Serventi F, Massawe A, **Henke O.** (2019). Repetitive Cancer Training for Community Health Care Workers: An Effective Method to Strengthen Knowledge and Impact on the Communities. Results from a Pilot Training at Kilimanjaro Region, Tanzania. J Cancer Educ 36(3), 470-47. (IF: 1,645); doi: 10.1007/s13187-019-01648-6.
4. Alwash Z*, **Henke O*,** Serventi F, Kanthelhardt E. (2019). Staff Perspectives Towards Challenges in a Newly Established Cancer Centre in Tanzania: A Qualitative Study. J Glob Oncol (5):1-8. (IF: 1,47); doi: 10.1200/JGO.18.00246.
5. Leak SA, Mmbaga LG, Mkwizu EW, Mapendo PJ, **Henke O**. (2020). Hematological Malignancies in East Africa – Which cancers to expect and how to provide services. PLoS ONE 15(5): e0232848 (IF: 3,24); doi: 10.1371/journal.pone.0232848.
6. **Henke O**, Mapendo PJ, Mkwizu EW, Lecoutre P. (2020). Early molecular response in East African Philadelphia chromosome positive chronic myeloid leukaemia patients treated with Imatinib and barriers to access treatment. *e*cancer, 14:1091 (IF: 2,08); doi: 10.3332/ecancer.2020.1089.

*geteilte Erstautorenschaft

Inhaltsverzeichnis

Abkürzungsverzeichnis

AIDS	Acquired Immunodeficiency Syndrome
BMC	Bugando Medical Centre
BRCA	Breast Cancer Gene
CCC	Cancer Care Centre
CDs	übertragbare Krankheiten (communicable diseases)
CHW	Community Health Worker
CLL	Chronische Lymphatische Leukämie
CML	Chronische Myeloische Leukämie
DALYs	Disability-adjusted Life Years
DHCW	Dispensary Health Care Worker
FGD	Fokusgruppen-Diskussion
HIC	High-income country/countries
HIV	Humanes Immundefizienz Virus
HL	Hodgkin Lymphom
HPV	Humanes Papilloma Virus
KCMC	Kilimanjaro Christian Medical Centre
LMIC	Low-and-middle-income country/countries
MC	Multiple Choice
MSI	Mikrosatelliteninstabilität
MM	Multiples Myelom
µl	Mikroliter
NCDs	Nicht-übertragbare Krankheiten (non-communicable diseases)
NGO	Non-governmental organisation
NHL	Non-Hodgkin-Lymphom
nl	Nanoliter
OR	Odds Ratio
ORCI	Ocean Road Cancer Institute
PBCR	population based cancer registries
SDG	Sustainable Development Goals
SLL	Small Cell Lymphoma

SSA	Sub-Sahara Afrika
TKI	Tyrosinkinase-Inhibitoren
VIA	Visual Inspection with Acetic Acid
WHO	World Health Organization

2. Einleitung

Krebserkrankungen galten lange Zeit fast ausschließlich als eine Herausforderung für Länder mit hohem Einkommen (high-income countries; HIC) und kamen in der Wahrnehmung der Wissenschaft und Organisationen der Entwicklungszusammenarbeit im globalen Süden nicht oder allenfalls nur am Rande vor (Pezzatini et al., 2007; Parkin et al., 2014). Mit der zunehmenden Beherrschung übertragbarer Krankheiten (communicable diseases; CDs) und den damit stetig sinkenden negativen Auswirkungen dieser Krankheiten auf die Bevölkerung (siehe Abb. 1), richtet sich der Fokus zunehmend auf Krebserkrankungen und andere nicht-übertragbare Krankheiten (non-communicable diseases; NCDs). NCDs sind mittlerweile eine große Herausforderung für die Gesundheitssysteme der Länder mit niedrigem und mittlerem Einkommen (low- and middle-income countries; LMIC) geworden (Malekzadeh et al., 2020). Die Diagnosestellung, Behandlung und Nachsorge sind komplex und in der Regel kostenintensiv und die Prävention der NCDs erfordern Lifestyle-Änderungen, die in der Umsetzung herausfordernd sind (Ndubuisi, 2021).

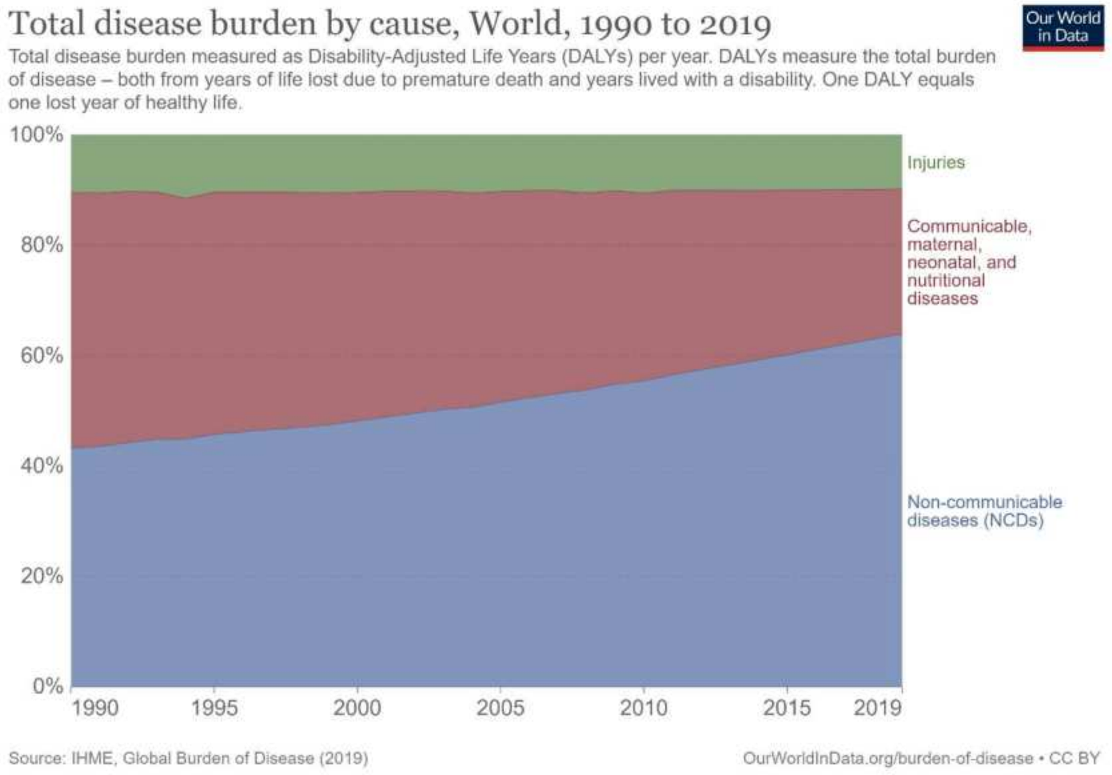


Abbildung 1: DALYs (disability adjusted life years) nach Krankheitsgruppen im zeitlichen Verlauf (Roser et al. 2021)

Die vorliegende Habilitationsschrift widmet sich dem Themenkomplex der Krebserkrankungen in LMIC am Beispiel des ostafrikanischen Landes Tansania und wird neben einer Zusammenfassung der einschlägigen Literatur die eigenen Forschungsleistungen in den Bereichen Health Services und klinischer Medizin aufzeigen und sie in Zusammenhang mit dem aktuellen Stand der Forschung in den globalen Kontext setzen.

Globale Epidemiologie von Krebserkrankungen

Im Jahr 2020 lag die globale Inzidenz von Krebserkrankungen bei 19.292.789 und die Mortalität im gleichen Jahr bei 9.958.133 (IARC, 2020). Während der Anteil der LMIC an der globalen Inzidenz bei unter 60% liegt, beläuft sich der Anteil der Mortalität in diesen Ländern auf über 70% (IARC, 2020) (siehe Abb. 2 und 3). Das Risiko an einer Krebserkrankung zu Versterben liegt demnach in den LMIC höher als in HIC und so finden sich beispielsweise die weltweit höchsten altersbereinigten Krebsmortalitätsraten unter Frauen in den Ländern Malawi, Mongolei, Papua-Neuguinea, Samoa, Serbien und Simbabwe (WCRF, 2020). Die Inzidenz von Mammakarzinomen beispielsweise liegt in HIC 2,3fach höher als in LMIC, während die bevölkerungsbezogene Mortalitätsrate in diesen Ländern jedoch 1,4fach höher ist als in HIC (IARC, 2020).

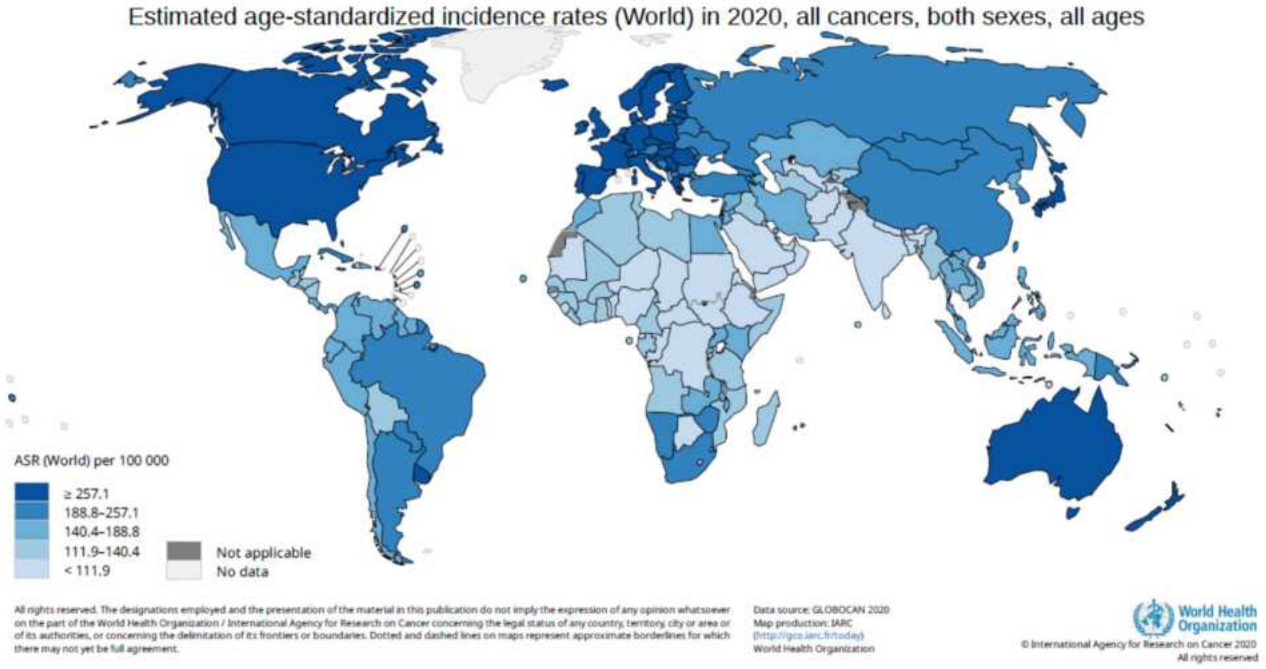


Abb. 2: Altersbereinigte globale Inzidenz von Krebserkrankungen (IARC, 2020)

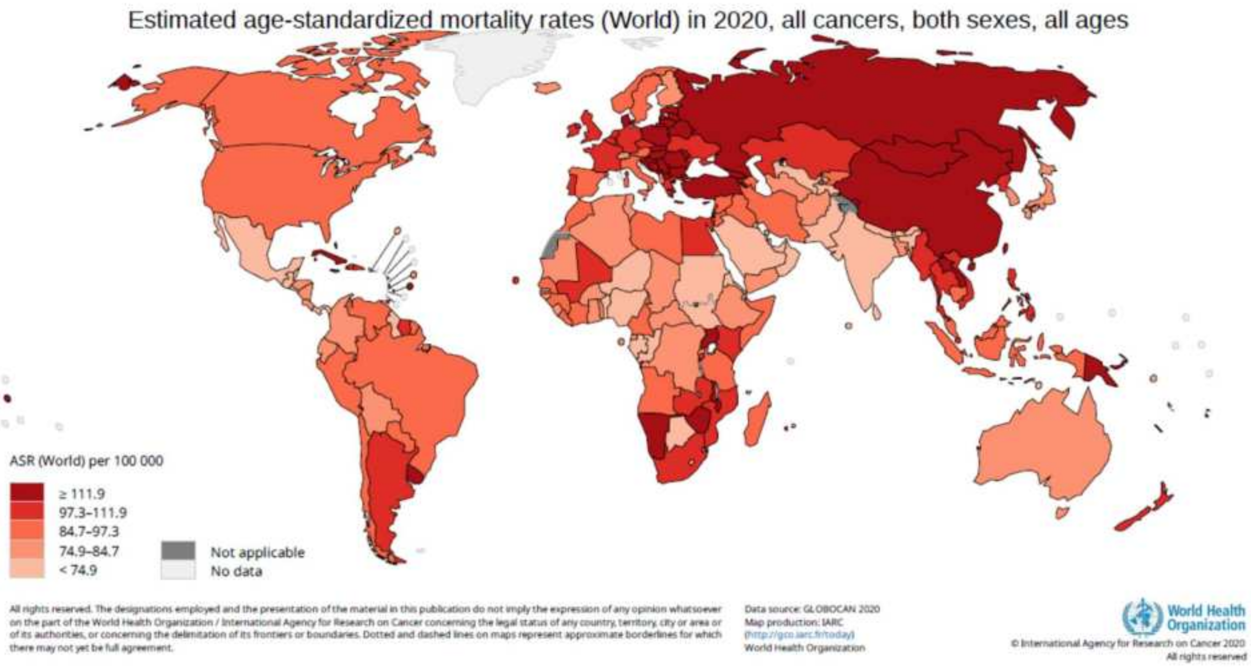


Abb. 3: Altersbereinigte globale Mortalität von Krebserkrankungen (IARC, 2020)

Die Projektionen für das Jahr 2040 erwarten eine Zunahme der Krebsinzidenzen und -mortalitäten in Afrika um 89,1% und 92,9%, in Zentral- und Südamerika um 65,6% und 77,3% und in Asien um 59,2% und 69,7%. Die Inzidenz in Europa wird um geschätzte 21,0% steigen, bei einer 29,2%igen Steigerung der Mortalität (IARC, 2020).

Diese Daten, die von der *International Agency for Research on Cancer* (IARC), der Abteilung für Krebserkrankungen der Weltgesundheitsorganisation (WHO), regelmäßig veröffentlicht werden, fußen in LMIC in erster Linie auf Schätzungen und müssen entsprechend vorsichtig interpretiert werden (IARC, 2022). Basis dieser Schätzungen bilden die bevölkerungsbezogenen Krebsregister (*population based cancer registries*, PBCR), die insbesondere in Sub-Sahara Afrika (SSA) mit vielen Herausforderungen konfrontiert sind, wie beispielsweise schwache Gesundheitssysteme, fehlende Bevölkerungszensus und lückenhafte Dokumentationen der Krebsfälle (Omonisi et al., 2020). Zudem sind die Schätzungen zur Mortalität durch die hohen Raten an verlorenen Daten in der Nachverfolgung geprägt, die fast 50% erreichen können (Freeman et al., 2016). In der IARC Publikation *Cancer Incidences in Five Continents Vol. XI* aus 2021 (IARC, 2021) betonen die Autorinnen und Autoren, dass die Registerdaten aus LMIC aufgrund vieler fehl- und unterdiagnostizierter Krebserkrankungen unvollständig sind. Die Fehl- und Unterdiagnosen wiederum sind in den insgesamt schwachen Gesundheitssystemen und den bestehenden ökonomischen Verhältnissen begründet. Fehlende epidemiologische Expertise in vielen Ländern in SSA tragen weiter zu der Datenunsicherheit bei (Hamdi et al., 2021). Der Blick auf entitätsbezogene Schätzungen, durch systematische Reviews oder *modelling*, weisen auf bislang deutliche unterschätzte Prävalenzen und Inzidenzen von Krebserkrankungen in SSA hin (Arhin et al. 2022; Gesink et al., 2020; Ward et al., 2019).

Die beschriebenen Unterschiede in den Inzidenz- und Mortalitätsraten haben mannigfaltige Gründe. Wie ich in einer im Oktober 2022 publizierten Übersichtsarbeit im der Fachzeitschrift Forum der Deutschen Krebsgesellschaft (Henke, 2022b) beschrieben habe, sind es vor allem die im Nachfolgenden genannten Themen, die die onkologische Versorgung in ressourcenarmen Ländern bestimmen.

Späte Diagnosestellung

Die Diagnosestellung der Krebserkrankungen in LMIC in einem späten Krankheitsstadium (Brand et al. 2019; Nnaji et al. 2021; Rick et al. 2021) ist der wohl wichtigste Grund für die höheren Mortalitätsraten. Umfassende und valide Daten aus bevölkerungsbezogenen Krebsregistern fehlen bezüglich der Krankheitsstadien in LMIC zwar weitegehend (Siddiqui und Zafar 2018), jedoch zeigen entitätsbezogene Reviews oder Daten aus einzelnen Behandlungszentren, dass der Anteil an Stage III- und IV-Erkrankungen bei Erstdiagnose zwischen 40% und 80% liegt, mit höheren Anteilen in SSA und niedrigeren in Zentral- und Südamerika (Noronha et al. 2019; Gnanamuttupulle et al. 2021; de Lemos et al. 2019). Gründe dafür liegen in Irrglauben und Unwissenheit über Krebserkrankungen (Rick et al. 2021; Stewart et al. 2018; Agodirin et al. 2021), mangelnden finanziellen Ressourcen der Patientinnen und Patienten (Wassie und Fentie, 2021; Rick et al. 2021; Agodirin et al. 2021), Behandlungen außerhalb des konventionellen Gesundheitssystems (Wassie und Fentie, 2021; Friebel-Klingner et al., 2021) und Verzögerungen in der Diagnostik durch die Gesundheitsdienstleister selbst (Rick at al. 2021; Wassie und Fentie, 2021).

Infektionen und Krebs

Ein weiterer Unterschied zwischen HIC und LMIC liegt in der Verteilung der Krebsentitäten. Die Rate an infektionsbedingten Krebserkrankungen ist in den tropischen und sub-tropischen Ländern deutlich höher. Dies zeigt sich eindrücklich in der Rate der HPV- (Humanes Papilloma Virus) Positivität, die bei Frauen in SSA weltweit am höchsten ist (Kombe et al., 2021). Watson-Jones at al. haben beispielsweise eine HPV-Prävalenz von 73% unter sexuell aktiven jungen Frauen in Tansania beschrieben (Watson-Jones et al, 2013). Auch unter jungen ugandischen Frauen lag sie in einer anderen Studie mit 75% vergleichbar hoch (Banura et al., 2010). In diesen Ländern, wie in vielen anderen Ländern in SSA auch, ist daher entsprechend Gebärmutterhalskrebs die häufigste oder zweithäufigste Krebsentität bei Frauen (IARC, 2022). Das HPV wird für insgesamt rund 15% aller Krebsfälle in SSA, einer Studie von Parkin et al. (Parkin et al., 2020) zufolge, verantwortlich gemacht. In dieser Studie, die auf afrikanischen Krebsregisterdaten aus dem Jahr 2018 beruht, wurde der Anteil an infektionsbedingten Krebserkrankungen in SSA auf 28,7% geschätzt, während es global ca. 13% sind (de Martel et al., 2020). Neben HPV haben vor allem die Hepatitis B- und C-Viren, das Ebstein-Barr-Virus, das Kaposi-Sarcoma associated herpes virus (KSHV) sowie das Humane Immundefizienz Virus (HIV) ihren Anteil an der Karzinogenese (Parkin et al., 2020). Bakterielle und parasitäre Infektionen spielen nach Parkin et al. insgesamt eine deutlich geringere Rolle, sind jedoch für einzelne Entitäten entscheidend. *Schistosoma haematobium* zum Beispiel ist für rund die Hälfte aller über 33.000 neudiagnostizierten Harnblasenkarzinome in Afrika verantwortlich (Saginala et al, 2020).

Genetische Unterschiede und Umwelteinflüsse

Auch die Exposition zu anderen externen Faktoren tragen in LMIC in einem höheren Maße zur Karzinogenese bei als in HIC. Laut *The Cancer Atlas* fördern Holz und Kohle, hauptsächlich genutzt in Innenräumen zum Kochen, bis zu 285.000 Bronchialkarzinome/Jahr in LMIC (American Cancer Society, 2023). Die Arsenbelastung des Trinkwassers lässt in mehreren LMIC vor allem das Risiko ansteigen, Haut-, Lungen- und Blasenkarzinome zu entwickeln (ebd.). Insgesamt ist die berufsbedingte Exposition zu karzinogenen Noxen in LMIC problematischer einzuschätzen, da Arbeitsschutzvorschriften unzureichend sind, gänzlich fehlen oder nicht durchgesetzt werden (McCormack und Schütz, 2012).

Neben Umweltfaktoren sind es auch genetische Unterschiede, die zu den inter-ethnischen und inter-regionalen Unterschieden beitragen. Eine nigerianische Studie zum Beispiel zeigte auf, dass unter den untersuchten Nigerianerinnen 7,1% bzw. 3,9% BRCA1 und BRCA2 Mutationen trugen. Im Vergleich waren es 1,4% und 2,6% bei afro-amerikanischen Frauen (Adedeji, 2021). Dies könnte die höhere Rate an *tripple* *negative breast cancer* erklären, die in mehreren Studien auf dem afrikanischen Kontinent beschrieben wurden (Hercules et al., 2022; Gnanamuttupulle et al., 2021; Thakur et al., 2018).

Eine retrospektive Untersuchung von 90 histopathologischen Proben aus Ghana konnte einen erstaunlich hohen Prozentsatz an Mikrosatelliteninstabilität (MSI) von 61% (41% MSI-high, 20% MSI-low) bei Patientinnen und Patienten mit kolorektalen Karzinomen finden (Raskin et al., 2013). In einer nigerianischen Kohorte von 64 Patientinnen und Patienten waren es noch 28,1% mit MSI-high (Alatise et al., 2021).

Bis heute sind genetische Studien in LMIC jedoch eine Ausnahme. Rotimi et al. haben in einem Review beschrieben, dass sich weltweit gerade einmal 0,02% aller Onkologie-bezogenen Publikationen in den Jahren 1990 bis 2019 auf Krebsgenetik bzw. Genomik auf dem afrikanischen Kontinent bezogen haben (Rotimi et al. 2021). Auch für den Bereich der *precision oncology* (personalisierte Medizin) haben mehrere Publikationen die Ungleichheit zwischen HIC und LMIC beschrieben und vor einer weiteren Spaltung der Medizin durch mangelnde finanzielle Ressourcen in LMIC gewarnt (Wahida et al., 2023; Drake et al., 2018). Auf der anderen Seite bieten die neuen Verfahren, wie beispielsweise die Nanopore-Sequenzierung, in ressourcenarmen Ländern aber auch Perspektiven, da sie helfen können, fehlende konventionelle diagnostische Kapazitäten zu überbrücken (Legason et al., 2022). Folgerichtig haben Pramesh et al. in einem Beitrag in Nature Medicine die stärkere Forschung in LMIC auf dem Gebiet neuer Technologien zur Bekämpfung der steigenden Krebsinzidenzen gefordert (Pramesh et al, 2022).

Fachkräfte und Bestrahlungseinheiten

Ungeachtet der bereits bestehenden Herausforderungen durch Krebserkrankungen in LMIC und der zu erwartenden Steigerung der Inzidenzen, gibt es nur wenige oder gar keine Spezialistinnen und Spezialisten in diesen Ländern (Fadelu und Shulman, 2018), was dazu führt, dass die vorhandenen Fachkräfte deutlich mehr Fälle schultern müssen als ihre Kolleginnen und Kollegen in HIC. Einer Erhebung von Mathew zufolge, hatten die meisten Länder SAAs im Jahre 2018 nur eine einstellige Zahl an Onkologinnen und Onkologen (Mathew, 2018), so dass in diesen Ländern eine Fachkraft auf mehrere tausend neudiagnostizierte Krebspatienten kam. Zum Vergleich kamen in Deutschland im Jahr 2020 bei einer Inzidenz von 628.519 (IARC, 2020) 124,51 neue Krebspatientinnen und -patienten auf eine Fachkraft (einbezogen alle

Fachärzte für Onkologie, Strahlentherapie und mit Schwerpunkt in gynäkologischer oder pädiatrischer Onkologie (Bundesärztekammer, 2020)). Eine Online-Umfrage unter 1115 onkologischen Fachkräften zeigte die Unterschiede in der Arbeitsbelastung der Fachkräfte in LMIC auf (Fundytus et al., 2017), die im Median 425 Patientinnen und Patienten pro Jahr behandelt haben (40% mit über 500 Konsultationen/Jahr) und damit eine signifikant höhere Arbeitsbelastung hatten als Fachkräfte in HIC mit 175 Fällen im Median (7% über 500 Konsultationen/Jahr). Eine andere Studie stellte zudem eine geringere Arbeitszufriedenheit unter afrikanischen Onkologinnen und Onkologen fest sowie die Notwendigkeit in ihrer Routinearbeit Patientinnen und Patienten mit sämtlichen Krebsentitäten zu behandeln (Vanderpuye et al., 2019). Ein systematisches Review aus dem vorletzten Jahr, in dem neben den Fachärztinnen und Fachärzten für Onkologie auch die globale Verfügbarkeit von Fachkräften für Pathologie, Medizinphysik und Strahlentechnik untersucht wurden, zeigte, dass der Fachkräftemangel der letztgenannten Spezialisten in LMIC noch ausgeprägter ist (siehe Abbildung 4) (Trapani et al. 2021).

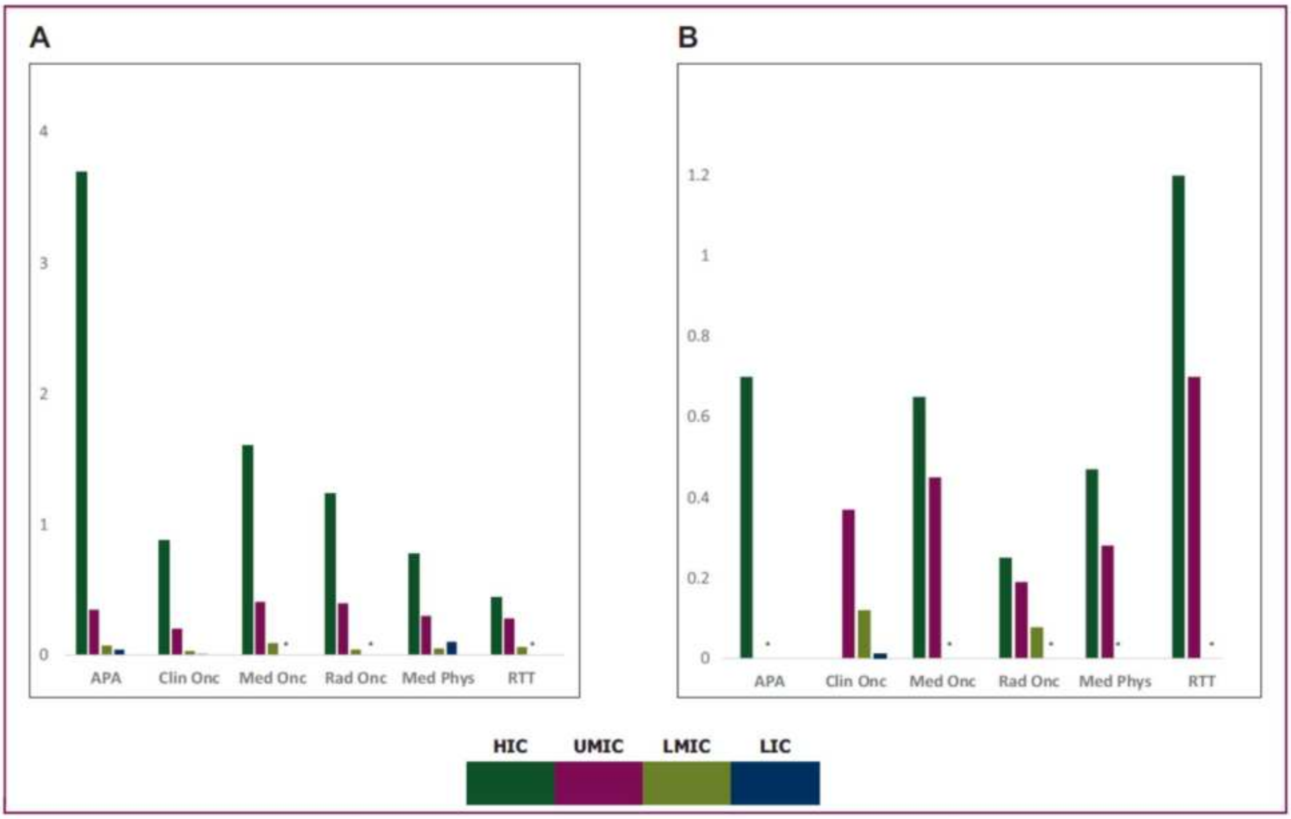


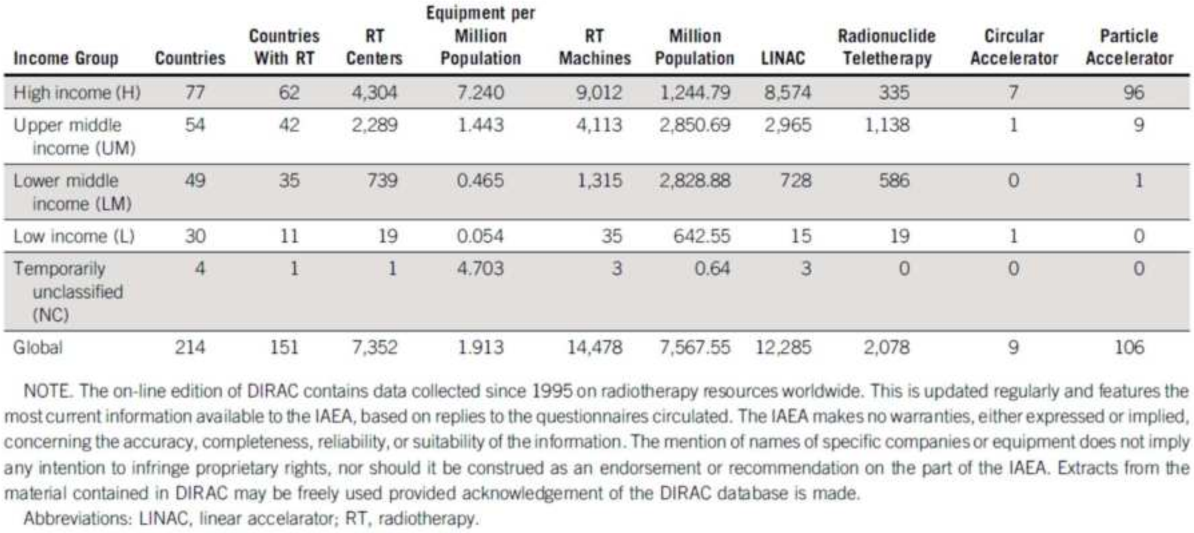
Figure 2. Distribution of the estimated median ratios of health providers per population (A) and per cancer patients (B).
APA, anatomic pathologist; Clin Onc, clinical oncologist; HIC, high-income country; LIC, low-income country; LMIC, lower-middle-income country; Med Onc, medical oncologist; Med Phys, medical physicist; Rad Onc, radiation oncologist; RTT, radiation therapy technician; UMIC, upper-middle-income country.
* Estimate not available.

Abb. 4: Onkologische Fachkräfte pro 100.000 Bevölkerung (A) und pro 100 Krebsfälle (B) nach Einkommenssituation der Länder (Trapani et al. 2021)

Fast gänzlich unbeachtet bleibt in der Literatur bislang die Bestandsaufnahme von onkologischen Pflegefachkräften und Pharmazeuten (Fadelu und Shulman, 2018), die ebenso entscheidende Rollen in der onkologischen Versorgung übernehmen.

Während der Bedarf an Ausbildungen in der Onkologie und angrenzenden Bereichen in LMIC offensichtlich sehr groß ist, fehlen jedoch aktuelle Erhebungen, die den Stand von Ausbildungsprogrammen und Initiativen abbilden (Karim et al. 2021). Abudu et al. haben in einer Befragung der *National Cancer Institutes - Designated Cancer Centers* in den USA festgestellt, dass 47% der Zentren *Global Oncology* Programme haben, diese aber zu über 75% auf Forschungsprojekte fokussieren und nur weniger als ein Drittel der Programme zum Kapazitätsaufbau (sog. *Capacity Building*) in LMIC beitragen (Abudu et al., 2019). Dabei sind es vor allem internationale Kooperationen, die zur Kapazitätsentwicklung und damit zur Verbesserung der onkologischen Versorgung in LMIC beitragen können, wie das *National Cancer Programme* in Ruanda gezeigt hat (Stulac et al., 2015).

Neben dem Fachkräftemangel ist vor allem die Ausstattung mit Bestrahlungseinheiten eine große Herausforderung. Keine Bestrahlungseinheiten gibt es in der Hälfte der afrikanischen Länder und in Lateinamerika erfüllt lediglich Uruguay die Empfehlung der Internationalen Atomenergiebehörde (IAEA) von 1 Megavolt pro 250.000 Einwohner (Grover et al., 2015). Abdel-Whab et al. haben im vorletzten Jahr die letzte globale Bestandsaufnahme publiziert, die vor dem Hintergrund der rapide ansteigenden Krebsinzidenz den immensen Bedarf in LMIC noch einmal unterstreicht (siehe Tabelle 1) (Abdel-Wahab et al., 2021).



Income Group	Countries	Countries With RT	RT Centers	Equipment per Million Population	RT Machines	Million Population	LINAC	Radionuclide Teletherapy	Circular Accelerator	Particle Accelerator
High income (H)	77	62	4,304	7.240	9,012	1,244.79	8,574	335	7	96
Upper middle income (UM)	54	42	2,289	1.443	4,113	2,850.69	2,965	1,138	1	9
Lower middle income (LM)	49	35	739	0.465	1,315	2,828.88	728	586	0	1
Low income (L)	30	11	19	0.054	35	642.55	15	19	1	0
Temporarily unclassified (NC)	4	1	1	4.703	3	0.64	3	0	0	0
Global	214	151	7,352	1.913	14,478	7,567.55	12,285	2,078	9	106

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Abbreviations: LINAC, linear accelarator; RT, radiotherapy.

Tabelle 1: Radiotherapie-Einheiten nach Einkommen-Kategorie der Länder (Abdel-Wahab et al., 2021).

In einer bemerkenswerten Publikation in The Lancet Oncology haben Atun et al. bereits 2015 die immensen finanziellen Aufwendungen für den Aufbau der Radiotherapie in LMIC mit 184 Milliarden US-Dollar beziffert (Atun et al., 2015), gleichzeitig aber berechnet, dass damit 26,9 Millionen Lebensjahre in LMIC gerettet werden würden und somit zu einem Nettonutzen von 278,1 Millionen US-Dollar in den Jahren 2015 bis 2035 führen würden. Mit bis zu sechs US-Dollar Ertrag für jeden investierten US-Dollar, führen die Investitionen nicht nur zur adäquaten Therapie einer großen Anzahl von Patientinnen und Patienten, sondern auch zu einem wirtschaftlichen Benefit in den LMIC (ebd.).

Palliativmedizin

Aufgrund des hohen Anteils an Stage III- und IV-Krebserkrankungen ist ein palliativmedizinisches Angebot in LMIC ein wichtiger Bestandteil der onkologischen Versorgung. Der *World Palliative Care Alliance* zufolge leben 76% der Patientinnen und Patienten mit einem Bedarf an palliativmedizinischer Versorgung in LMIC (WPCA, 2020). In Afrika hatten jedoch nur 5% der Bedürftigen Zugang zu einer palliativmedizinischen Versorgung, stellten Downing et al. 2015 fest (Downing et al., 2015). Gerade einmal 7% des weltweiten Morphins wird in LMIC konsumiert (WPCA 2020). Dabei kommt der Palliativmedizin aber gerade in den Ländern mit niedrigem Einkommen neben der symptomatischen Therapie ein weiterer wichtiger Aspekt zu: Anderson und Grant beschrieben 2017 den Effekt auf die ökonomische Situation der betroffenen Familien. Dabei stellen sie fest, dass die Abwesenheit einer palliativmedizinischen Versorgung zu signifikanten Ausgaben für Therapien führt, die von der Familie geschultert werden müssen und zu Veräußerung von Viehbestand, Land, Ersparnissen und zur Herausnahme der Kinder aus den Schulen führe, um Schulgebühren zu sparen und Gesundheitsausgaben damit zu decken. Armut wird so perpetuiert und an die Folgegeneration weitergegeben (Anderson und Grant 2017). Die Reduktion von Gesundheitsausgaben durch ein palliativmedizinisches Angebot bei Patientinnen und Patienten mit fortgeschrittenen Krebserkrankungen, konnte jüngst in Malawi im Rahmen einer prospektiven Vergleichsstudie nachgewiesen werden (Bates et al. 2021). Die Gesundheitsausgaben konnten um 36% gesenkt werden. Katastrophale Gesundheitsausgaben (definiert als Ausgaben von mehr als 20% des Gesamthaushalteinkommens) kamen in der Interventionsgruppe, die eine palliativmedizinische Versorgung erhielt, zu 47% vor und in der Vergleichsgruppe zu 69% (ebd.).

Situation in der Vereinigten Republik Tansania

Tansania liegt im südlichen Ostafrika und ist ein Flächenstaat mit 947.000 km² und einer Bevölkerung von ca. 61,5 Millionen Einwohnern und gehört zu den LMIC (World Bank 2022). Das Bevölkerungswachstum lag 2021 bei 2,81% und gehört damit zu den Ländern mit den höchsten Raten weltweit (ebd.). Im Jahr 2020 lag die Prävalenz von Krebserkrankungen bei 73.303, die Inzidenz bei 40.464 und die Mortalität bei 26.946 (IARC 2020). Eine retrospektive Studie hat die krankenhausbasierte altersbereinigte Mortalitätsrate für die Jahre 2006 bis 2015 auf 47,8 pro 100.000 Einwohner beziffert (Lyimo et al. 2020), was insgesamt höher liegt als die Daten der IARC aus den PBCR. Die häufigste Krebsentitäten unter Tansanierinnen sind Zervixkarzinome, Mammakarzinome, kolorektale Karzinome und Kaposi-Sarkome. Bei Tansaniern werden zumeist Prostatakarzinome, Ösophaguskarzinome, Kolorektale Karzinome und Kaposi-Sarkome diagnostiziert. Die Schätzungen der IARC gehen von einer Verdopplung der Krebsinzidenzen bis 2040 aus (siehe Abb. 5) (IARC 2020).

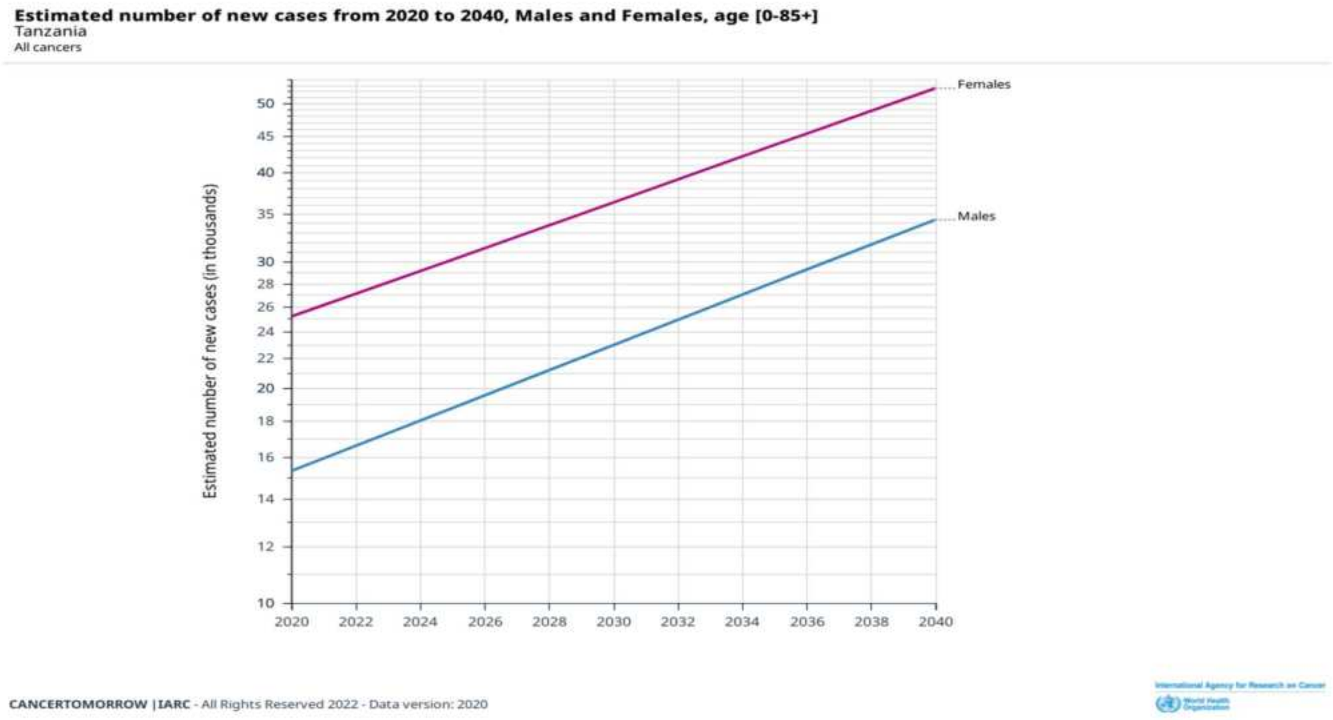

Abb. 5: Entwicklung der Krebsinzidenz in Tansania bis 2040, nach Geschlecht (IARC, 2020)

Aktuell gibt es in Tansania drei öffentliche Krankenhäuser, in denen Krebsbehandlungen angeboten werden: Das *Ocean Road Cancer Institute* (ORCI) in Dar Es Salaam als staatliches Krebsinstitut seit 1996, das *Oncology Department* des Bugando Medical Centre seit 2015 (BMC), das *Cancer Care Centre* des Kilimanjaro Christian Medical Centre seit 2016 (KCMC) und dem Benjamin Mkapa Hospital seit 2019. Radiotherapie wird bis dato nur im ORCI und BMC angeboten. Das Aga Khan Hospital in Dar Es Salaam und die Besta Polyclinic ergänzen das Behandlungsangebot im privaten Sektor (Makene et al. 2022).

Eine wachsende Anzahl wissenschaftlicher Publikationen beschäftigt sich in den letzten Jahren mit Krebserkrankungen in Tansania und berichtet über epidemiologische und klinische Erkenntnisse (Olson et al. 2020, Gnanamuttupulle et al. 2021, Herman et al. 2020, Schroeder et al 2018, Lyimo et al. 2020). Andere Publikationen setzen sich mit Public Health Aspekten zum Zugang und Akzeptanz von Behandlungsangeboten (Bateman et al 2019, Mugassa et al. 2019, Yeates et al. 2020) oder dem Wissen um Krebserkrankungen bzw. mit der Gesundheitskompetenz der Bevölkerung (Weng et al. 2020, Chao et al. 2020).

Als eines der wenigen Länder der Region, ist in Tansania die Facharztausbildung bzw. ein Masterprogramm in Onkologie an der *Muhimbili University of Health and Allied Sciences* in Dar Es Salaam möglich (Rubagumya et al. 2019). Zudem wurden vergleichsweise früh ein *National Cervical Cancer Prevention and Control Strategic Plan 2011 – 2015* und später eine *National Cancer Control Strategy 2013 – 2022* von der Regierung verabschiedet (ICCP 2022).

Trotz einer Vorreiterrolle auf vielen Gebieten der onkologischen Versorgung, bestehen mannigfaltige Hürden für eine flächendeckende onkologische Versorgung (Rick et al. 2021, Makene et al. 2022).

Im Ergebnisteil stelle ich die eigenen Forschungsergebnisse dar, die aus Projekten während meiner Zeit als Facharzt für Hämatologie und Onkologie am KCMC im Norden Tansanias entstanden sind. Dabei beleuchten diese Forschungen die Gesundheitskompetenz in Bezug auf Krebserkrankungen in der Allgemeinbevölkerung und unter dem Gesundheitspersonal und fokussieren auf Lücken in der klinischen Versorgung von Patientinnen und Patienten mit hämatologischen Neoplasien.

3. Ergebnisteil

Henke O, Bruchhausen W, Massawe A. Use of Herbal Medicine Is Associated With Late-Stage Presentation in Tanzanian Patients With Cancer: A Survey to Assess the Utilization of and Reasons for the Use of Herbal Medicine. JCO Glob Oncol. 2022 Jul;8:e2200069.

Zielsetzung der Arbeit: Es sollte der Anteil der Krebspatientinnen und -patienten untersucht werden, die am KCMC zusätzlich zur konventionellen Behandlung auch *„herbal medicine“* (Naturheilkunde) nutzen. Die Frage war zudem, ob dies einen Einfluss auf eine späte Diagnosestellung hat.
Methoden und Ergebnisse: Eine semistrukturierte fragebogenbasierte Umfrage an 302 Krebspatientinnen und -patienten wurde durchgeführt. Neben soziodemografischen (Alter, Geschlecht, Schulbildung, Beruf, Wohnort) und klinischen Merkmalen (Entität und Stadium) wurde nach der Anwendung von *„dawa ya mitishamba“* (am ehesten mit „Naturheilkunde“ zu übersetzen) und der Sequenz der verschiedenen Behandlungen gefragt: Anwendung der Naturheilkunde vor, nach oder parallel zur konventionellen Behandlung. Zudem wurde nach den Gründen für die Anwendung der Naturheilkunde gefragt. Der Fragebogen beinhaltete 30 Fragen mit binären, geschlossenen und offenen Antworten. Letztere wurden inhaltsanalytisch ausgewertet und die Antworten kategorisiert; die binären und geschlossenen Antworten deskriptiv ausgewertet und mit dem Erkrankungsstadium korreliert. Es folgte eine Berechnung der Odds Ratio (OR) und des p-Wertes, um statistische Signifikanzen darzustellen.
70,5% der Befragten wendeten Naturheilkunde für die aktuelle Krebserkrankung an. Davon haben 67,1% zuerst Naturheilkunde und anschließend konventionelle Medizin angewendet, 24,9% nutzten beide Verfahren parallel und 7,5% begannen mit konventioneller Medizin. Stratifiziert nach Krankheitsstadien, haben Patientinnen und Patienten im Stadium IV häufiger Naturheilkunde als erste Behandlung angewendet (70.6%; Stadium III 57,2%; Stadium II 58,1%, Stadium I 55,6%). Dieser Unterschied ist statistisch signifikant mit einer OR von 12,000 und einem p-Wert von 0,00383.

Als häufigsten Grund für die Anwendung von Naturheilkunde gaben die Befragten „Glaube an Heilung durch Naturheilkunde“ an, gefolgt von „Hoffnung auf Besserung der Symptome“ und „Fehlende konventionelle Krebsbehandlungsangebote“ sowie „Tradition“.

Schlussfolgerungen: Die Mehrheit der Befragten nutzte Naturheilkunde vor der Schulmedizin. Dabei gab es keine Unterschiede zwischen Schulbildung, Berufen, Wohnort oder Art der Krebserkrankung. Jedoch zeigen die Ergebnisse, dass die Anwendung von naturheilkundlicher Medizin als erste Behandlungsoption zu einem höheren Risiko führt, erst später, in einem metastasierten Stadium, diagnostiziert zu werden. Diese Ergebnisse bestätigen Vermutungen, dass alternative Behandlungsmethoden zu dem Problem der *„late stage presentation“* in Tansania beitragen. Die Gründe für die Anwendung der Naturheilkunde („Heilung durch Naturheilkunde“) deckt zudem Lücken in dem Wissen um Krebserkrankungen und der Gesundheitskompetenz der Befragten auf.

HEALTH SERVICES RESEARCH

original reports

Use of Herbal Medicine Is Associated With Late-Stage Presentation in Tanzanian Patients With Cancer: A Survey to Assess the Utilization of and Reasons for the Use of Herbal Medicine

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abstract

PURPOSE In Tanzania, patients with cancer present late with advanced stages. Among other reasons, the use of herbal medicine (HM) might contribute to delay in diagnosis and treatment. This study aims to understand the utilization of HM and the reasons for its' use.

METHODS A semistructured 30-item questionnaire with closed- and open-ended questions was applied to a cohort of patients with cancer at Kilimanjaro Christian Medical Centre. Content analysis was performed for answers to open-ended questions.

RESULTS Three hundred two patients were interviewed, 50.9% males and 49.1% females. The mean age was 64 years. 71.6% were in stages III/IV. 70.5% patients used HM and 67.1% started conventional medicine after stopping HM, 7.5% started HM after conventional medicine, and 24.9% combined both. Stage IV patients used HM as first line significantly more often in comparison: stage I 55.6%; II 58.1%; III 57.2%; and IV 70.6%. 77.5% did not tell their doctors about the use of HM. Commonest reasons to use HM were belief in cure, hope of symptom relief, lack of cancer services, and tradition.

CONCLUSION The majority of patients used HM before consulting a doctor, which contributes to stage IV presentation. Use of HM alongside with chemotherapy is mostly not known to the treating physician and may lead to interactions. These findings must alert health care workers and health policymakers to further foster health education about cancer and its treatment. Further research is needed to understand the wide use of HM among Tanzanian patients with cancer and the role that traditional and spiritual healers play in the field of cancer care.

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BACKGROUND

Cancer diseases are a growing burden in Tanzania and sub-Saharan Africa (SSA) as a whole[1] and will continue to affect larger swathes of the population in the future. Tanzania had a prevalence of 73,303 cancer cases in 2020 with an annual incidence of 40,464 and 26,945 cancer-related deaths.[2] Three cancer treatment facilities exist in the country with a population of almost 60 million, and barriers to access treatment in this setting include long distances to receive diagnosis and treatment, high out-of-pocket expenditures, and low level of knowledge among patients and health care providers about cancer.[3,4]

Apart from these impediments to receive medical attention in low- and-middle-income countries, it is known that patients with cancer worldwide use traditional and herbal medicine (HM) generally on a large scale[5] and in SSA, this is a critical component of health care.[6] The use of traditional and HM among patients with cancer in SSA has been studied in a few countries only and display inhomogeneous findings, from Nigeria, where 34% of patients with cancer use it, to 74% in Ethiopia.[7] As most of the patients use alternative medicine before consulting a medical doctor (respectively a conventional health care facility),[8] it is likely that it contributes to the high number of late-stage presentation of patients with cancer in SSA.[3,9,10] But, data confirming this assumption are lacking.

We conducted this study to understand the utilization of HM among patients with cancer attending the Cancer Care Centre (CCC) at Kilimanjaro Christian Medical Centre (KCMC) and the reasons behind their choice to identify possible interference with early

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Why do Tanzanian patients with cancer use herbal medicine (HM) and does the use influence time to presentation?

Knowledge Generated

Our survey revealed that 70% of patients with cancer use HM for their current cancer disease because they believe in cure through HM, expect symptoms relief, and because of lacking cancer services in their proximity. Most patients use HM before seeking care at a hospital, which leads to significant higher proportion presenting in stage IV disease compared with those who first consulted a conventional health facility ($P = .0013$).

Relevance

Our survey proofed the assumption that the use of alternative medicine leads to late-stage presentation in cancer diseases. The high proportion of patients using HM before seeking care at a hospital is alarming and reflects the deep-rooted tradition of HM. Efforts must be taken to educate patients on the relevance of timely presentation and treatment initiation of cancer diseases.

presentation of cancer diseases and treatment. A better understanding of the use of HM in Tanzania should also serve to shape health education and individual counseling of patients.

METHODS

Participants have been recruited between May and July 2018. A convenient sampling of patients with cancer visiting the CCC at KCMC for either clinic or treatment appointments have been invited to participate.

KCMC is the referral and university hospital in Northern Tanzania, located in the city of Moshi, and serves a catchment area of approximately 12 million people, reaching into neighboring Kenya. The CCC was established in 2016 and is at present the third cancer treatment facility in the country and the only one in the northern zone of the country.

A semistructured 30-item questionnaire with closed-ended, binary, multiple choice, and open-ended questions was applied. Seven items documented sociodemographic variables (age, sex, occupation, marital status, level of education, district of residency, and tribe), six items were directed to the current cancer disease and treatment, and 17 items were directed to the use of HM (Table 1). The Swahili term used to ask for HM was *dawa ya mitishamba*, which is equivalent to *HM or medicinal plants* and describes fresh plant products as well as processed powder from HMs. The survey was conducted by a trained and specialized nurse in palliative care, and a prephase with five patients secured the applicability of the questionnaire. The interviews were conducted in a separate room at CCC to secure privacy.

Answers to closed-ended and multiple choice questions have been coded, and bivariate analyses have been performed where indicated. A content analysis of the open-ended questions (reasons to use HM) has been performed and categories developed.

Ethical approval was sought and granted by the Ethical Review Board of the Kilimanjaro Christian Medical University College. A consent form has been signed by all participants. The participants were equipped with a telephone number of the study nurse in case of further questions or seeking advice or help after the interviews. We conducted the study in accordance with the Helsinki Declaration of the World Medical Association.

RESULTS

In total, 302 participants were interviewed; sex was balanced, with 154 (50.9%) males and 148 (49.1%) females. The average and mean age was 64 years, and 59 (19.5%) lived in urban and 242 (80.1%; one missing) in rural areas. The majority of participants were farmers (176; 58.3%), and teachers and other government employees (35; 11.6%). Two hundred four participants were married (67.6%), 49 were widowers (16.2%), 33 were single (10.9%), and 16 (5.3%) were divorced.

The level of education ranged from no education (32; 10.6%), primary school only (157; 51.9%), secondary education (37; 12.3%), to postsecondary education (71; 23.5%; five missing).

The most common type of cancer was breast cancer (82; 27.2%), GI cancer (61; 20.2%), prostate cancer (58; 19.2%), lymphoma (including multiple myeloma; 38; 12.6%), Kaposi sarcoma (18; 5.9%), gynecologic cancer (12; 3.9%), and other entities (32; 10.6%).

Fifteen patients (4.9%) were in stage I at the time of interview, 50 (16.6%) in stage II, and 82 patients in the stages III and IV (27.2%). Seventy-three patients did not know their stage (24.2%).

Two hundred eleven patients have ever used HM (69.9%) before being diagnosed with the current cancer disease. Two hundred thirteen patients use HM in the current disease: 193 (63.9%) daily, eight (2.6%) weekly, nine (3.0%) occasionally, and three patients (1.0%) only one time (Fig 1).

TABLE 1. Comparison of Patients Who Use HM for the Current Cancer Disease Daily, Weekly, or at Least Occasionally, or Used It Only Once or Never

	Use of HM			
Variable	**Yes (n = 210[a])**	**No (n = 92[a])**	**OR (CI)**	***P***
Age groups, years				
≤ 30	12	0	116.49874 (1.07907 to 7,491.11740)	**.01929**
31-40	16	5	1.43505 (0.47334 to 4.63979)	.49219
41-50	26	18	0.58092 (0.28665 to 1.18157)	.10337
51-60	50	23	0.93750 (0.51197 to 1.72338)	.82400
61-70	49	23	0.91304 (0.49785 to 1.68062)	.75440
71-80	38	13	1.34258 (0.64757 to 2.82051)	.39730
> 80	19	10	0.81571 (0.34169 to 1.97770)	.62088
Sex				
Males	104	50	0.82415 (0.48937 to 1.38716)	.44021
Females	106	42		
Residency				
Rural	172	70	1.46100 (0.77078 to 2.76076)	.21122
Urban	37	22		
Rural late stage	99	34		
Urban late stage	18	12	1.94118 (0.78336 to 4.78845)	.11253
Occupation				
Farmer	124	52	1.10912 (0.65558 to 1.87549)	.68202
Government employees	20	15	0.54035 (0.24883 to 1.17802)	.09021
Others	66	25	1.22833 (0.68965 to 2.19601)	.45829
Level of education				
No education	25	7	1.60031 (0.62649 to 4.25068)	.29017
Primary school	113	44	1.21651 (0.71808 to 2.06144)	.43941
Secondary school	28	9	1.38272 (0.59040 to 3.31972)	.42332
Postsecondary school	42	29	0.52347 (0.28882 to 0.94957)	**.02180**
Cancer stages				
I	9	6	0.66892 (0.20681 to 2.21805)	.46016
II	30	20	0.61417 (0.30501 to 1.23942)	.14037
III	51	31	0.63634 (0.34449 to 1.17549)	.12134
IV	67	15	2.82889 (1.41321 to 5.72408)	**.00137**
Cancer types				
Breast cancer	54	28	0.88895 (0.49457 to 1.60098)	.67527
GI cancer	42	19	1.07368 (0.55737 to 2.07962)	.82058
Prostate cancer	43	15	1.48489 (0.74001 to 3.00931)	.23358
Lymphoma/MM	24	14	0.79204 (0.36731 to 1.72059)	.52221
Kaposi sarcoma	10	8	0.57413 (0.19955 to 1.66834)	.25582
Gynecologic tumors	9	3	1.45665 (0.34953 to 6.97720)	.57804

Abbreviations: HM, herbal medicine; MM, multiple myeloma; OR, odds ratio.

[a] Missing numbers to 302 because of missing answers.

In addition to the use of HM, 77 patients (25.5%) consulted a traditional healer for the current cancer disease. Out of those 77, 20 (26.0%) patients have visited the traditional healer once (26.0%), 22 (28.6%) twice, and 35 (45.5%) several times.

The majority of patients who used traditional medicine in the current cancer disease (n = 213) have started conventional medicine (CM) after stopping HM (143 [67.1%]), 16 started HM after finalizing conventional treatment (16 [7.5%]), and 53 patients (24.9%) combined HM and

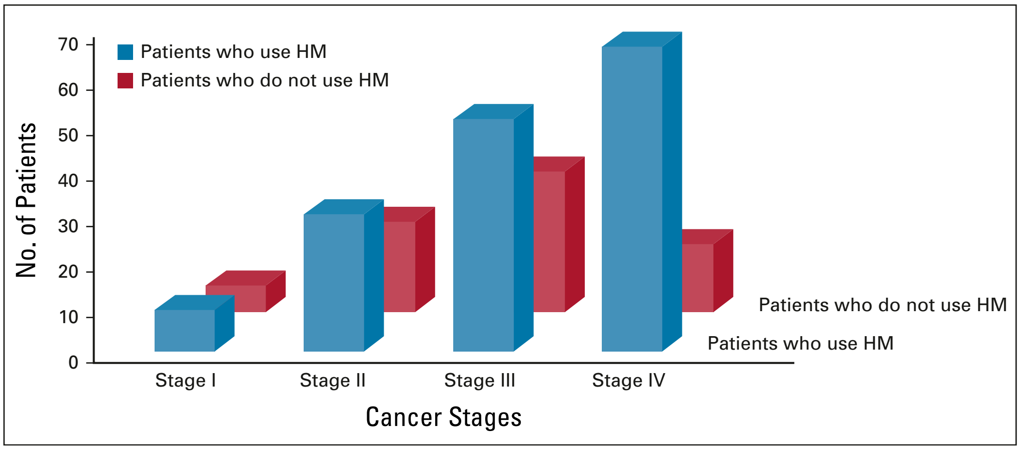

FIG 1. Use of HM according to disease stages. HM, herbal medicine.

conventional treatment. Stratified to cancer stages, patients in stage IV have used HM before CM in 70.6%, HM/CM at the same time in 27.9%, and CM before HM in 1.5%. Compared with the other stages (stage I: 55.6%; 11.1%; 33.3%; stage II: 58.1%; 9.7%; 32.3; stage III: 57.2%; 24.6%; 17.7%), this difference is significant with an odds ratio of 12.000 (CI, 1.53303 to 258.38659; *P* = .00383).

One hundred fifty-seven (73.7%) out of the 213 patients using HM for the current cancer disease reported about a poor level of satisfaction with HM, 52 (24.4%) report a good satisfaction, and three (1.4%) patients had excellent satisfaction. Corresponding to the level of satisfaction, 157 (73.7%) patients would not use HM for a cancer disease again nor recommend HM for cancer diseases but 55 (25.8%) would do.

One hundred sixty-five patients (77.5%) did not tell their oncologists about the use of HM.

One hundred five patients got their information about HM from family members, 131 from friends, 78 through media, 42 from other patients, and 35 from health care workers.

The answers were categorized after content analysis into eight categories: believe in cancer cure through HM (mentioned by n = 96), hope of symptom relief (n = 34), lack of cancer services in their area (n = 32), because of tradition (n = 23), recommendations by others (n = 9), to reduce the side effects of chemotherapy (n = 8), high expenses (n = 5), and fear of operation (n = 3; Fig 2).

DISCUSSION

This survey was conducted to understand the use of HM among patients with cancer in Northern Tanzania. Almost two third of the patients indicated to have used or still use HM for the current cancer disease that has let them to attend the cancer care clinic. Hope for cure and tradition have been mentioned as the most common reasons to use HM followed by lack of cancer services.

An unexpected finding in our cohort was the finding of high utilization of HM among patients younger than 30 years, which stands in stark contrast to a household survey from South Africa in 2011, where age was adversely associated with the use of traditional healers.[11] Although our results must be taken with caution because of the few numbers (n = 12) of interviewees in this group, the fact that all these patients indicated the use of HM deserves some thoughts and discussion. Sayed et al[12] examined young Kenyans (median age 22 years in women and 31 years in men) by means of focus group discussions and questionnaires. Although the indication of the use of traditional healers was generally very low in the questionnaires, the focus group decision revealed insights into believes of being bewitched, especially in not common diseases such as cancer.[12] Another important factor for the use of alternative medicine was the proximity of healers and hence their easy access.

It must be noted from our findings that 70% used HM for the current cancer disease but only a quarter of the patients consulted a traditional healer. Hence, using HM must be influenced by other factors. Hereby, friends and media as sources of information have been named by the interviewees in our cohort. Corresponding to this, Asuzu[13] stated in a 1994 published article from Ibadan in Nigeria that the most common source of information about HIV are media. In a recent publication from South Africa about health promotion and social media, a major challenge mentioned was "it allows information to spread far and fast […] irrespective of the source of information."[14] We do believe that the increasing and constant availability of social media information about health and medicine has a huge impact especially on younger patients and might explain our findings. Traditional medical practitioners use media on a large scale to advertise their products and do this in a manner that lacks both medical and business ethics, according to a study analyzed the situation in South Africa, Mozambique, and Zimbabwe.[15] This, however, remains an assumption, and further research is needed to look closer to the relation of social media influence on patients with cancer.

The correlation of stage IV cancer disease and use of HM is—apart from the younger age group—the only significant

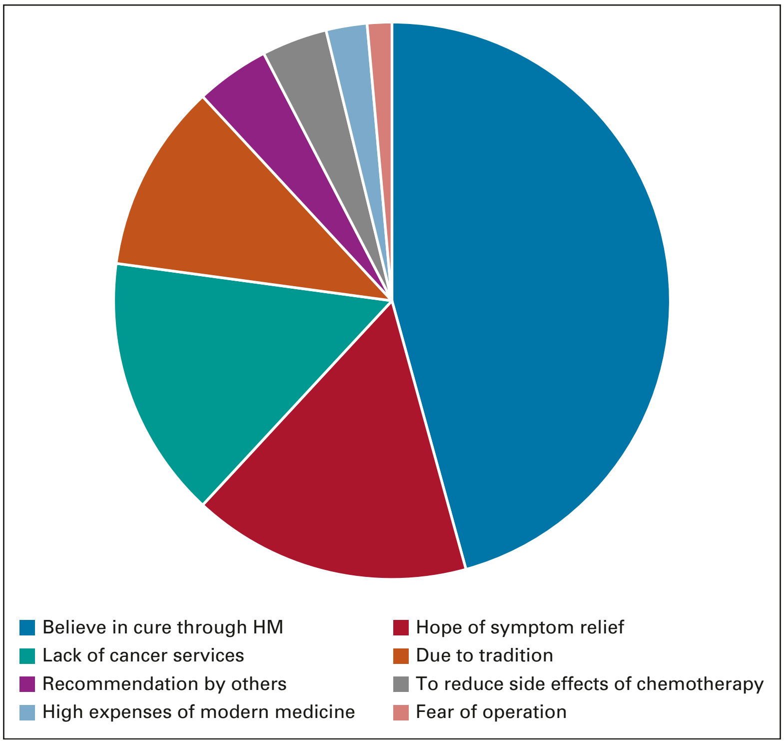

FIG 2. Reasons of the interviewed patients for the use of HM. HM, herbal medicine.

finding of our survey. Facing late-stage cancer diseases, patients often seek alternative treatment, often at the same time.[16-18] However, our findings show that more than 70% use HM before seeking medical attention in the CCC and only 2% started with CM before using HM (Fig 3). The authors understand this as a strong but also alarming evidence that HM distracts patients for a long time from being served in modern health facilities. This finding is supported by other studies from different countries.[9,19,20]

The scope of reasons given for the use of HM covers the whole range of motives and obstacles for seeking any form of therapy, from basic mental issues such as trust, habit, fear, or social pressure, to practical issues such as distances and finances. The Human Right to Health addresses most of these concerns as requirements by the AAAQ approach (Availability, Accessibility, Acceptability, and Quality), that is, that health care services must be available and accessible, including being affordable and culturally acceptable, and of sufficient quality.[21]

Although only a small number of our interviewees expressed that high expenses of modern medicine was a reason for using HM, it must be assumed that it is a considerable factor for treatment decisions, especially when the treatment goes beyond primary care. The studies mentioned in the introduction proved this point.[3,4] It has been also shown that an increase in treatment costs induces patients who had been open to biomedical services to return to traditional medicine.[22] The fact that many cancer medicines have been provided free of charge in the Centre during 2018 through donations might have led to mitigate the financial problem in our cohort.

The fact that patients from rural areas are more likely (odds ratio 1.46) to use HM than those from urban areas indicates the importance of availability and geographical accessibility of treatment in specialized centers.[10]

By far, the highest share in the survey has been the socially expected answers of sociocultural factors of own belief, recommendation, and tradition. Use of HM appears as the common way of life. Yet, HM is not a traditional, that is, ancient complex of fixed practices for dealing with unwanted states of health, but was formed in competition, imitation, and resistance with regard to the practices imported from the Global North.[23] Thus, it is not a mere matter of just being accustomed to traditional medicine but involves questions of constructing cultural identity and securing social cohesion, dealing with conflict, and coping with contingency. The majority of these concerns are not antimodern or anti-Western, but deeply connected to the ways of explaining misfortune, defending oneself against destructive forces. As CM does not address these existential issues, regarded as the ultimate causes of ill-health, a complementary action must be applied. These beliefs are expressed by the high number of interviewees stating that only HM can cure cancer. Furthermore, many patients started using both types of medicine simultaneously. This may also point out to the conviction that conventional cancer treatment cannot be sufficient for getting completely healed. And furthermore, some patients mentioned the use of HM to reduce the side effects of chemotherapy

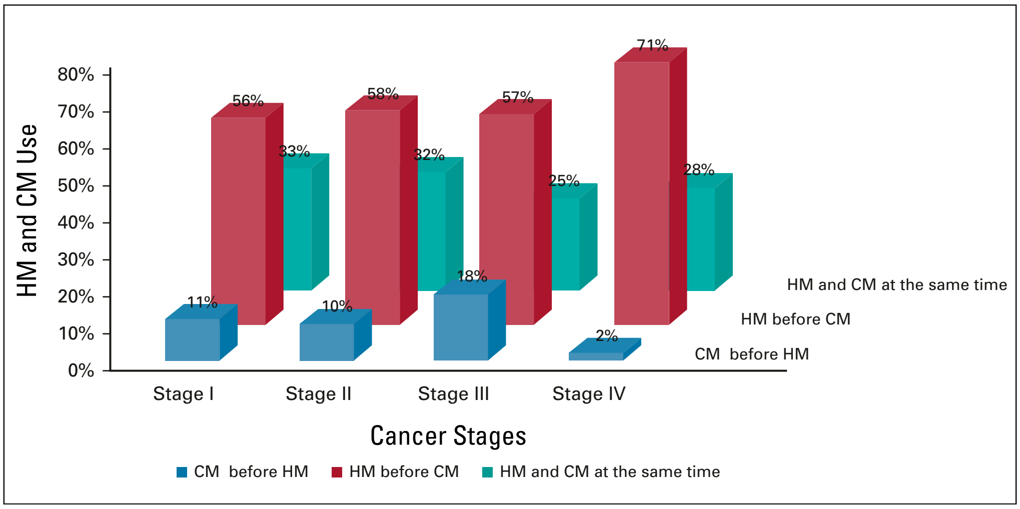

FIG 3. Sequence of using HM and CM according to stage of cancer disease. CM, conventional medicine; HM, herbal medicine.

treatment. This is also known as a common motivation for patients with cancer in different settings.[24-26]

The majority of the interviewed patients would not talk to their oncologists about the concurrent use of HM. This correlates with findings from other parts of the world, such as Korea, where Kang et al[27] revealed that 70% of the patients with cancer would not talk with the treating physician about the use and a Malaysian study with self-administered questionnaires displayed similar results,[28] as did studies conducted in African countries.[25,26] Patients would not relate this information to their doctors because they were not asked for it. Fear of telling the physician or the belief that HM has no side effects of interaction is also common in patients with cancer.[29]

In conclusion, the use of HM is generally high among patients with cancer in Northern Tanzania and most use it before consulting a medical doctor, which contributes to delay in diagnosing and eventually treatment of the cancer disease. The concurrent use of HM alongside chemotherapy is mostly not known to the treating physician and may lead to unwanted interactions. This finding must alert Tanzanian oncologists (and globally as other studies have shown) to thoroughly obtain the history of patients including the pointed question about HM use and the reasons behind it. Misconceptions about conventional cancer treatments must be responded by enhanced health education of the general population as no specific correlation with demographic characteristics can be identified, neither in our study nor in most of others.

This survey was physically conducted within the CCC's building. A bias toward social desirable answers is likely, which might indicate an even higher utilization of HM.

Furthermore, our study cannot distinguish within the highly diverse practices of traditional medicine, for example, whether the herbal treatment was combined with other rituals or what the role of traditional and spiritual healers has been in the decision for the use of HM. Future more qualitative studies should apply such differentiations to understand what precisely patients with cancer are looking for. This might also facilitate a dialogue with healers who provide HMs about referral and possible collaboration as well as a culturally sensitive health education and promotion for the general population. With the rising burden of noncommunicable diseases, such approaches may increase the urgently needed acceptance of timely and long-term treatment for health problems that start less obviously than many infectious diseases.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

Conception and design: Oliver Henke, Anna Massawe
Financial support: Anna Massawe
Administrative support: All authors
Provision of study materials or patients: Anna Massawe
Collection and assembly of data: Oliver Henke, Anna Massawe
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/go/authors/author-center.
Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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Henke A, Kluge U, Borde T, Mchome B, Serventi F, **Henke O**. (2021) Tanzanian women´s knowledge about Cervical Cancer and HPV and their Prevalence of positive VIA cervical screening results. Data from a Prevention and Awareness Campaign in Northern Tanzania, 2017 – 2019. Glob Health Action. Jan 1;14(1):1852780

Zielsetzung der Arbeit: In einer Querschnittsstudie sollte das Wissen über Gebärmutterhalskrebs und HPV von Frauen, die an Krebspräventions- und Aufklärungskampagnen in Tansania teilgenommen hatten, ermittelt werden. Zudem wurden die VIA Screening-Ergebnisse der teilnehmenden Frauen ausgewertet. Die Ergebnisse sollen dazu beitragen, Aufklärungskampagnen gezielter zu gestalten und die aktuelle Rate an Präkanzerosen unter Frauen in der Kilimanjaro Region darzustellen.

Methoden und Ergebnisse: 2192 Frauen wurden mittels Fragebogen interviewt und 2224 Frauen nahmen an der Gebärmutterhalskrebs-Früherkennung teil. Der Fragebogen basierte auf dem validierten *Cervical Cancer Awareness Measure* und wurde nach Expertinnen- und Experteninterviews kulturell und sozial angepasst. Das VIA-Screening wurde durch geschulte Fachkräfte durchgeführt und dokumentiert. Wenn indiziert erfolgte eine Kryotherapie vor Ort. Das Durchschnittsalter lag bei 44 Jahren, 75% kamen aus ländlichen Gegenden und 43% waren Kleinbäuerinnen. Das monatliche Durchschnittseinkommen betrug für 59% weniger als 50 US-Dollar. 56% hatten keine Krankenversicherung, 70% waren verheiratet und 39% hatten mehr als vier Kinder. 81% hatten bereits von Krebs gehört und 53% gaben an, es sei ein Problem in ihrer Gemeinde. Als Krebsursache gaben 43% genetische Mutationen an, 20% den Gebrauch von Kontrazeptiva, 14% Fluch, 5,8% Impfungen und 2,8% glaubten an eine direkte Übertragung durch Krebspatientinnen. Nur 22% der Befragten kannten Gebärmutterhalskrebs. Dieses Wissen war assoziiert mit einem höheren Einkommen, Alter zwischen 45 und 54 Jahren und dem Vorhandensein einer Krankenversicherung. Herkunft oder Anzahl der Kinder spielte dabei keine Rolle. 16,3% der städtischen und 9,7% der ländlichen Bevölkerung nahm zuvor bereits an einem Screening teil. 75% der Befragten hatten niemals über eine HPV-Infektion gehört und 51% wussten nicht, dass es eine Impfung gibt. Das Wissen um HPV korrelierte positiv mit Bildung, höherem Einkommen, Krankenversicherung und vorherige Teilnahme an einem Screening. 2,6% der Frauen, die am Screening teilnahmen, waren HIV-positiv. 3,1% waren VIA positiv.

Schlussfolgerungen: Diese nicht bevölkerungs-repräsentativen Ergebnisse weisen auf ein geringes Wissen über Gebärmutterhalskrebs und HPV sowie auf Irrglauben über Krebserkrankungen hin. Verglichen mit anderen Studien aus Tansania zeigt sich aber ein etwas höheres Wissen, insbesondere im ländlichen Bereich, was auf die vergleichsweise gute Versorgung durch Gesundheitseinrichtungen in der Kilimanjaro Region zurückzuführen sein könnte. Darauf lässt auch die geringe Rate an positiven VIA Screenings schließen, die – verglichen mit anderen Studien aus Tansania – am geringsten war und mit einer geringen HIV-Rate korreliert. Vermehrte und gezieltere Aufklärungskampagnen sind vonnöten, um das Wissen um HPV-Impfungen und Früherkennungsprogrammen zu verbessern. Screening-Angebote sollten auch in primären Gesundheitseinrichtungen angeboten werden, um die Teilnehmerinnenrate zu erhöhen.

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Tanzanian women´s knowledge about Cervical Cancer and HPV and their prevalence of positive VIA cervical screening results. Data from a Prevention and Awareness Campaign in Northern Tanzania, 2017 – 2019

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ABSTRACT

Background: 14.9 million women (≥15 years) in Tanzania are at risk of developing cervical cancer. Limited cancer care facilities, prevention programs and sparse knowledge among community members and healthcare workers contribute to late-stage presentation leading to a high mortality rate.

Objective: This study aims to scientifically accompany prevention and awareness campaigns (PrevACamp) in northern Tanzania in its real-world settings to obtain (1) a better understanding about cervical cancer and HPV knowledge amongst female PrevACamp participants and (2) to determine the prevalence of pre-cancerous lesions among women undergoing cervical cancer VIA screening.

Method: Cross-sectional survey among PrevACamp attendees in two regions in Northern Tanzania. Two data collections tools were used: Questionnaires and clinical data from VIA screening. Data were collected from October 2017 to March 2019.

Results: 2,192 PrevACamp attendees were interviewed and 2,224 received VIA screening. There was significant nescience on cervical cancer regardless of education level, resident status, or number of children as well as nescience on HPV in all age groups, especially in urban areas and misconceptions about cancer. Screening revealed VIA positivity rate of 3.1%.

Conclusion: There is an alarming lack of knowledge about cervical cancer and, to a lesser Extent, about HPV among the study participants. Having health insurance influenced the level of knowledge significantly. Outreach programs in rural areas appear to target the population in need of health education. Low positive VIA screening results are paralleled with lower HIV rates among the women. We assume that the high density of primary health care coverage in northern Tanzania contributes to these findings..

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Background

Cervical cancer is the fourth most common cause of cancer-related deaths with more than 300,000 cases per year worldwide [1,2]. Approximately 90% of all cervical cancer deaths occur in low- and middle-income countries (LMICs) [2]. In Sub-Saharan Africa (SSA), it is the second leading cause of cancer-related deaths among women [3] and in Tanzania, cervical cancer is the most frequently diagnosed cancer among women aged between 15 and 44 years [4]. The annual incidence of cervical cancer is 9,770 cases per 100,000 women with a mortality rate of 6,695 [4]. If no specific action is taken, Tanzania is estimated to have 12,416 new cervical cancer cases and 9,923 deaths per year in 2025 [5].

Comprehensive national screening programs may reduce the incidence and mortality rate from cervical cancer [6]. Limited access to these programs in LMICs increases the prevalence of advanced stages of the disease. This compares to high-income countries where primary and secondary prevention programs lead to early detection and increased survival rates [2,6]. Currently, the national cervical cancer screening programme in Tanzania uses VIA (visual inspection with acetic acid) as the standard screening procedure [7] which is available free of charge in government and church-based hospitals on different levels of care. Although, VIA has lower sensitivity and specificity compared to PAP smear and HPV testing [8], it remains the standard of care in many low income countries because of its single visit approach and the generally high prevalence of cervical cancer in these countries. PAP smears and HPV (human papillomavirus) tests are available in the zonal hospitals in Tanzania.

Human papillomavirus (HPV) type 16 and 18 cause 70% of cervical cancer and pre-cancerous cervical lesion cases [9]. The World Health

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Knowledge of cervical cancer and VIA screening outcome in Northern Tanzania

Organization (WHO) recommends the following measures to lower the burden of cervical cancer: (1) primary prevention (HPV vaccination for girls aged 9–14 years, so they are protected before they become sexually active), (2) secondary prevention (screening and treatment of pre-cancerous lesions), (3) tertiary prevention (diagnosis and treatment of invasive cervical cancer) and (4) palliative care [2].

In general, infection-related cancer occurs more often in SSA compared to other regions in the world [10]. Apart from HPV infections, women with human immunodeficiency virus (HIV) have a higher likelihood of developing cervical cancer [11]. The HIV-prevalence of women above 15 years of age in Tanzania is 4.6% [12] and affecting urban and rural areas alike. Nearly 80% are resulting from heterosexual transmission [13].

The 14.9 million women that are above the age of 15 years in Tanzania are at risk of developing cervical cancer [4]. Kilimanjaro Christian Medical Center (KCMC) hosts the only specialized cancer care facility in Northern Tanzania [14] with a catchment area of approximately 15 million people. The next available radiation unit is located 550 km away in Dar es Salaam, Tanzania´s largest city. The Tanzanian Ministry of Health and Social Welfare (MoHSW) implemented a National Cancer Control Strategy (NCCS), that targets cancer education in schools, HPV vaccination, health promotion and screening programs for high-risk populations [15].

In 2014, a schools-based HPV vaccination program supported by the GAVI-Alliance (Global Alliance for Vaccines and Immunization) was successfully piloted within the Kilimanjaro Region [16,17]. An increase in national vaccination programs for girls between 9 and 14 years is expected in the future [16], which will need support from prevention and awareness campaigns.

A lack of knowledge about preventive measures among the general population and healthcare workers hinders effective cervical cancer prevention and treatment [18,19] and must be considered when designing prevention strategies. It is known that knowledge gaps among health care workers and the general population lead to a higher mortality rate in LMICs [19,20]. Furthermore, differences in knowledge have been found between rural and urban areas in Tanzania [21,22], with generally lower knowledge in remote areas. However, evidence regarding cervical cancer and HPV knowledge as well as the prevalence of precancerous cervical lesions are sparse.

In 2017, the Cancer Care Centre (CCC) at KCMC launched Cancer Prevention and Awareness Campaigns (PrevACamps) in two Northern Tanzanian regions (Kilimanjaro and Arusha) covering the districts of Hai, Mwanga, Rombo, Moshi Urban, Arusha Urban, Moshi Rural, and Siha. The PrevACamps offer education seminars and screening programs for the communities, as well as training community health care providers to enhance their cancer awareness and knowledge. This study aims to scientifically accompany PrevACamp in its real world setting to obtain (1) a better understanding about cervical cancer and HPV knowledge amongst female PrevACamp participants and (2) to determine the prevalence of pre-cancerous lesions among the screened women. The study focuses on the differences between women living in rural and urban settings.

Methods

A cross-sectional study design among PrevACamp attendees was chosen. Two data collection tools were used: questionnaires and documented clinical data records from the mass screening during PrevACamps between October 2017 and March 2019. Cervical cancer screening was conducted by applying VIA [23] followed by cryotherapy where indicated. (Figure 1)

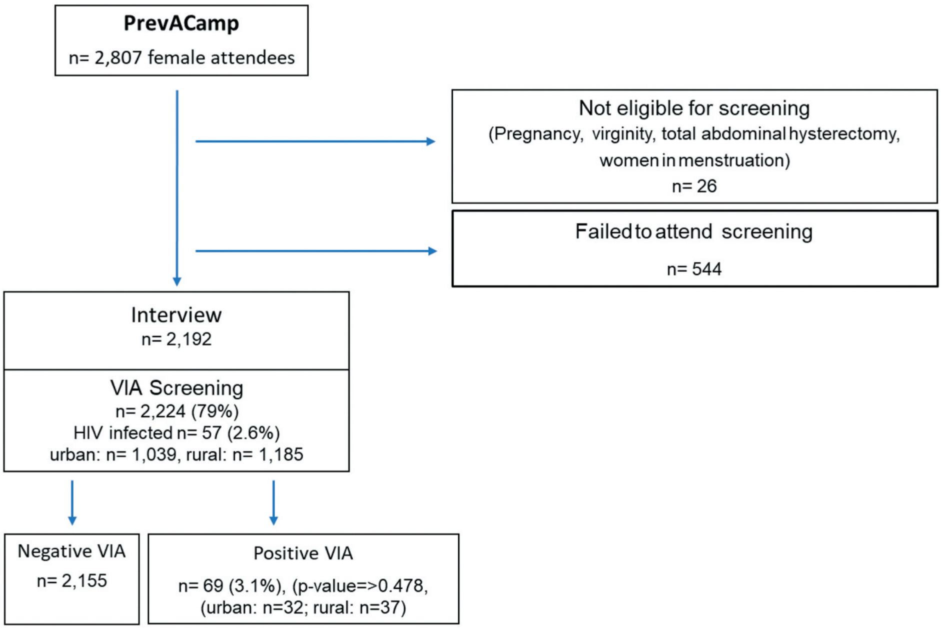
Study setting

Arusha (with a population of 1,694,310) and Kilimanjaro (1,640,087) Regions (districts of Hai, Mwanga, Rombo, Moshi Urban, Arusha Urban, Moshi Rural, and Siha) are characterized by rural and urban areas. The majority of inhabitants live from small-scale farming or day labor jobs and small businesses [24]. The PrevACamp events were conducted in either faith-based hospitals or health centers in the respective districts. The regional and district medical officers were involved in planning and conducting the events.

Study population and recruitment

The attendees were invited through loudspeaker cars, church announcements, and radio advertisements in the respective districts. Questionnaires: Interviewees were recruited from all PrevACamp attendees using convenience sampling of just arriving attendees. Trained interviewers informed all prospective interviewees about the purpose of the study and obtained consents.

VIA-screening: Cervical screening was offered to all female PrevACamp participants above the age of 18 years. Prior to screening, all women were informed by nurses about the screening process and possible results. Exclusion criteria were pregnancy, virginity, women with total abdominal hysterectomy (TAH), and women who were menstruating (Figure 1).



KCMC= Kilimanjaro Christian Medical Centre, PrevACamp= Prevention and Awareness Campaign, VIA= Visual inspection using acetic acid, LEEP= Loop Electrosurgical Excision Procedure

Figure 1. Flowchart of attendee´s recruitment.

KCMC = Kilimanjaro Christian Medical Centre, PrevACamp = Prevention and Awareness Campaign, VIA = Visual inspection using acetic acid, LEEP = Loop Electrosurgical Excision Procedure.

Data collection tools

Data collection tools were questionnaires and clinical data from the VIA screenings.

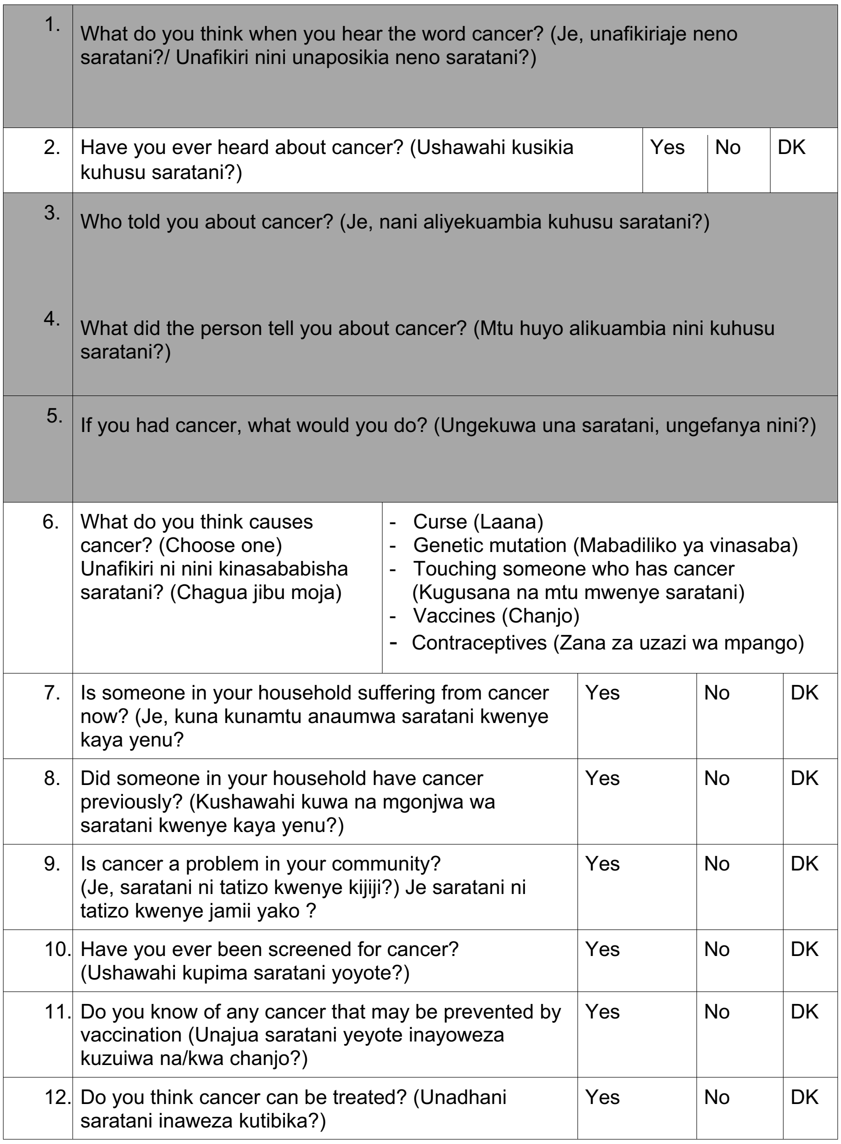
Questionnaires: Questions from the validated Cervical Cancer Awareness Measure (Cervical CAM) were selected [25]. After discussions with key informants, questions were rephrased, and additional questions were added for cultural and social adaptation into the Tanzanian setting. The questionnaire was developed in English and for- and back-translated by two independent Swahili speakers to assure the coequality of the Swahili questionnaire. The questionnaire was divided into five sections: (1) cancer knowledge, (2) risk factors, (3) early symptoms, (4) cancer beliefs, and (5) socio- demographic characteristics. The survey included in total 62 items: 22 closed responses (yes/no/I do not know), 14 open-ended, 9 multiple response questions and 17 questions about socio-demographic characteristics. Four questions were asked about cervical cancer knowledge and three questions about HPV knowledge.

Average interview time was 25 minutes and the questionnaires were administered by 2 male and 3 female interview-trained health care professionals. 2 pilot phases were conducted for evaluation of feasibility and comprehension of the questions. (Figure 2)

VIA screening: Each woman, who enrolled in the VIA screening program, was documented in a register ‘Cervical Cancer screening register’ from the MoHSW. Information recorded in a reporting form included: serial number, name of clients, address, phone number, age, first sexual contact, HIV status, date last menstrual period and screening results, use of cryotherapy and referral for Loop Electrosurgical Excision Procedure (LEEP) or other procedures. VIA screenings were performed by 6 gynecologists and specialized nurses who underwent VIA training in the past and who had longstanding experience in applying VIA screening.

Data analysis

(Questionnaire, VIA screening): For data entry and analysis SPSS Version 23.0 was used: Continuous variables were summarized using the mean, standard deviation, median and interquartile range. Categorical data were summarized using frequency and percentage measures. The data were stratified by urban and rural areas. The comparison of the difference between the social demographic characteristics was conducted using odds ratio (OR) and 95% CIs. Chi-square was used to find possible associations between sociodemographic factors with women’s knowledge of cervical cancer, HPV, and status ‘never screened for cervical cancer’. The ‘level of knowledge of cervical cancer’ was determined by categorizing responses in to knowledgeable (at least 2 out of 4 correct answers) and nescience (less than 2 correct answers). The level of knowledge of HPV was defined as knowledgeable, if 2 out of 3 questions were correctly answered and nescience, if less than 2 questions were answered correctly.



1.	What do you think when you hear the word cancer? (Je, unafikiriaje neno saratani?/ Unafikiri nini unaposikia neno saratani?)			
2.	Have you ever heard about cancer? (Ushawahi kusikia kuhusu saratani?)	Yes	No	DK
3.	Who told you about cancer? (Je, nani aliyekuambia kuhusu saratani?)			
4.	What did the person tell you about cancer? (Mtu huyo alikuambia nini kuhusu saratani?)			
5.	If you had cancer, what would you do? (Ungekuwa una saratani, ungefanya nini?)			
6.	What do you think causes cancer? (Choose one) Unafikiri ni nini kinasababisha saratani? (Chagua jibu moja)	- Curse (Laana) - Genetic mutation (Mabadiliko ya vinasaba) - Touching someone who has cancer (Kugusana na mtu mwenye saratani) - Vaccines (Chanjo) - Contraceptives (Zana za uzazi wa mpango)		
7.	Is someone in your household suffering from cancer now? (Je, kuna kunamtu anaumwa saratani kwenye kaya yenu?	Yes	No	DK
8.	Did someone in your household have cancer previously? (Kushawahi kuwa na mgonjwa wa saratani kwenye kaya yenu?)	Yes	No	DK
9.	Is cancer a problem in your community? (Je, saratani ni tatizo kwenye kijiji?) Je saratani ni tatizo kwenye jamii yako ?	Yes	No	DK
10.	Have you ever been screened for cancer? (Ushawahi kupima saratani yoyote?)	Yes	No	DK
11.	Do you know of any cancer that may be prevented by vaccination (Unajua saratani yeyote inayoweza kuzuiwa na/kwa chanjo?)	Yes	No	DK
12.	Do you think cancer can be treated? (Unadhani saratani inaweza kutibika?)	Yes	No	DK

Figure 2. Questionnaire.

DK: don´t know, The questions highlighted in grey were not analyzed in this study.

Using the Tanzanian National Bureau of Statistics definitions, residency of participants was categorized as either ‘urban’ (Arusha and Moshi Urban) or ‘rural’ (all other sites) [26].

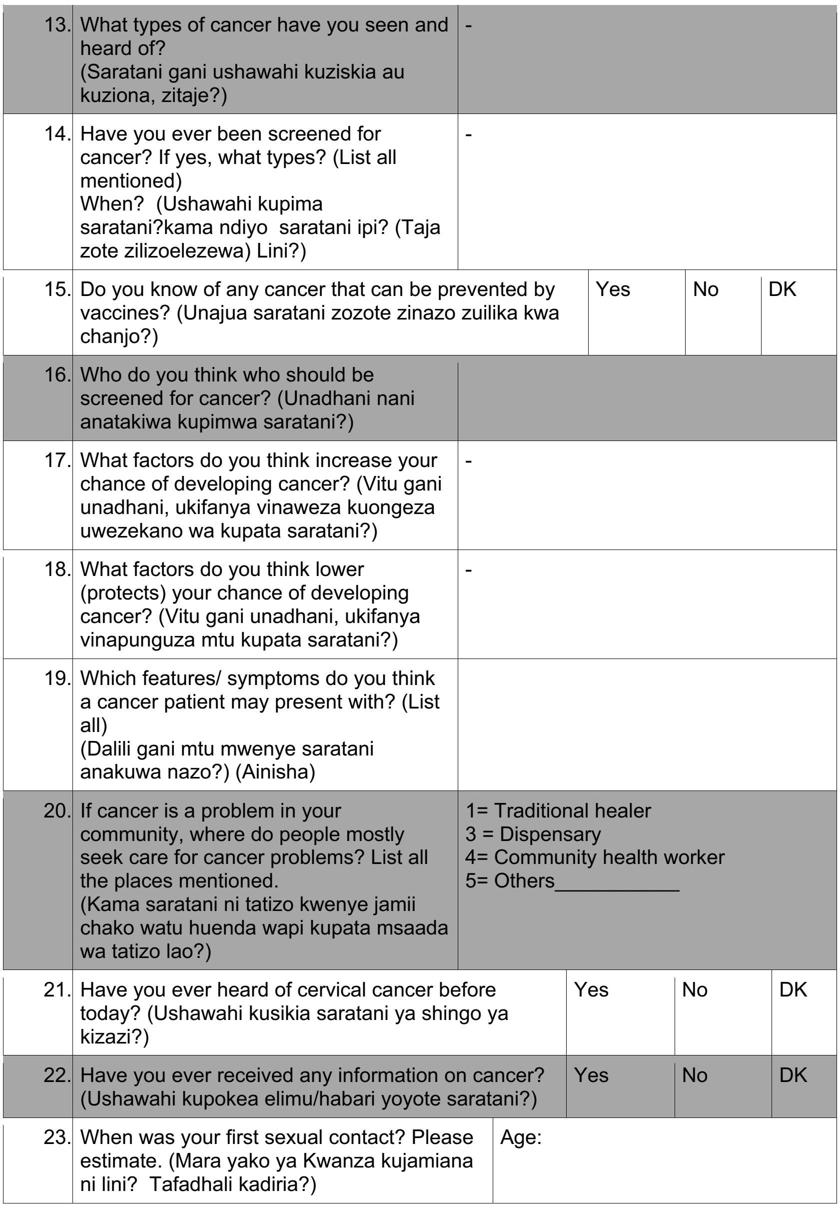
Ethical considerations

Ethical research clearance was secured from Kilimanjaro Christian Medical College in Moshi, Tanzania. Participants were informed about the purpose of the questionnaires and possible outcomes of VIA screening. Arrangements were made for treatment cost coverage in the event of positive screening results that would need to undergo therapy other than cryotherapy. Consent was given prior to data collection.

Results

The convenience sampling of all 2,807 female PrevACamps attendees included 2,192 interviewees and 2,224 screened women (Table 1). The sociodemographic characteristics of interviewed women displayed an overall mean age of 44 years (M = 44, SD = 15). 1,633 (75%) resided in rural areas. 944 (43%) were small-scale farmers, 453 (21%) were formally employed, and 531 (24.2%) had small businesses. The monthly income for 1,295 interviewees (59%) was lower than 50, USD 394 (18%) had a monthly income between 50 USD-$100, and 220 (10%) had between 100 USD-$250. 1,561 (71%) had a primary education or lower, 1,230 (56%) had no health insurance, 1,544 (70%) were married and 863 (39%) had more than 4 children.

Differences have been seen regarding residence status and sociodemographic factors: Rural women were significantly less likely to have a secondary education (n = 1,237; 76%; $p < 0.0001$) and less likely to be employed (n = 1,321; 81%; $p < 0.002$) than urban women. Reported first sexual intercourse under 15 years was more common in urban areas (n = 23; 4.2%) than in rural areas (n = 60; 3.8%).



13.	What types of cancer have you seen and heard of? (Saratani gani ushawahi kuziskia au kuziona, zitaje?)	-		
14.	Have you ever been screened for cancer? If yes, what types? (List all mentioned) When? (Ushawahi kupima saratani?kama ndiyo saratani ipi? (Taja zote zilizoelezewa) Lini?)	-		
15.	Do you know of any cancer that can be prevented by vaccines? (Unajua saratani zozote zinazo zuilika kwa chanjo?)	Yes	No	DK
16.	Who do you think who should be screened for cancer? (Unadhani nani anatakiwa kupimwa saratani?)			
17.	What factors do you think increase your chance of developing cancer? (Vitu gani unadhani, ukifanya vinaweza kuongeza uwezekano wa kupata saratani?)	-		
18.	What factors do you think lower (protects) your chance of developing cancer? (Vitu gani unadhani, ukifanya vinapunguza mtu kupata saratani?)	-		
19.	Which features/ symptoms do you think a cancer patient may present with? (List all) (Dalili gani mtu mwenye saratani anakuwa nazo?) (Ainisha)			
20.	If cancer is a problem in your community, where do people mostly seek care for cancer problems? List all the places mentioned. (Kama saratani ni tatizo kwenye jamii chako watu huenda wapi kupata msaada wa tatizo lao?)	1= Traditional healer 3 = Dispensary 4= Community health worker 5= Others___________		
21.	Have you ever heard of cervical cancer before today? (Ushawahi kusikia saratani ya shingo ya kizazi?)	Yes	No	DK
22.	Have you ever received any information on cancer? (Ushawahi kupokea elimu/habari yoyote saratani?)	Yes	No	DK
23.	When was your first sexual contact? Please estimate. (Mara yako ya Kwanza kujamiana ni lini? Tafadhali kadiria?)	Age:		

Figure 2. (Continued).

962 (44%) women had health insurance, with no remarkable difference between urban and rural regions (Table 1).

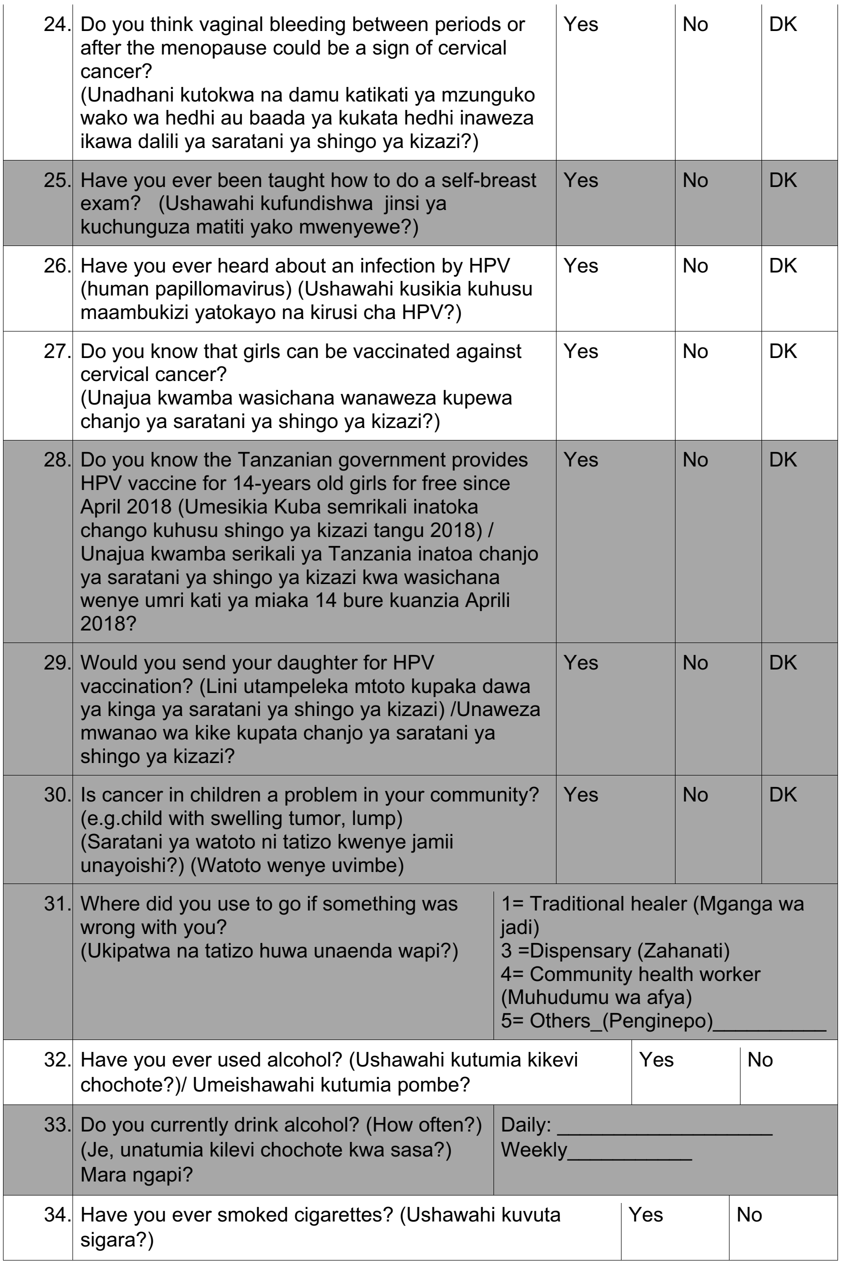
Cancer knowledge/misconceptions

The level of overall cancer knowledge is shown in Table 2. 1,785 (81%) of 2,192 women had heard about cancer with a noticeable difference between urban and rural areas. 1,151 (53%) of the interviewees reported that cancer is a problem in their community. 598 (27%) had a family history of cancer deaths (Table 2).

Out of 5 multiple choice questions about beliefs and misbeliefs about the etiology of cancer: 403 (43%) responded ‘genetic mutation’ as a cause of cancer, followed by use of contraceptives 288 (20%), curse 105 (14%), 54 (5.8%) vaccine, and direct contact with a cancer patient 26 (2.8%). Incorrect responses were positively associated with women living in rural settings (Table 2).

Knowledge of cervical cancer

The level of knowledge about cervical cancer was as follows: Among 2,192 women interviewed, 731(33%) reported that they had never heard of cervical cancer. 484 (22%) were knowledgeable (Figure 3). The following factors had a significant impact on cervical cancer knowledge: Women aged between 45–54 years, had a monthly income between 100 USD and 250 USD, and had health insurance (Figure 4). Education level, rural or urban residence, and the number of children were not associated with better knowledge of cervical cancer (Table 3). 16.3% women living in urban and 9.7% of women living in rural areas had been screened for cervical cancer prior to PrevACamp (Table 2).



24.	Do you think vaginal bleeding between periods or after the menopause could be a sign of cervical cancer? (Unadhani kutokwa na damu katikati ya mzunguko wako wa hedhi au baada ya kukata hedhi inaweza ikawa dalili ya saratani ya shingo ya kizazi?)	Yes	No	DK
25.	Have you ever been taught how to do a self-breast exam? (Ushawahi kufundishwa jinsi ya kuchunguza matiti yako mwenyewe?)	Yes	No	DK
26.	Have you ever heard about an infection by HPV (human papillomavirus) (Ushawahi kusikia kuhusu maambukizi yatokayo na kirusi cha HPV?)	Yes	No	DK
27.	Do you know that girls can be vaccinated against cervical cancer? (Unajua kwamba wasichana wanaweza kupewa chanjo ya saratani ya shingo ya kizazi?)	Yes	No	DK
28.	Do you know the Tanzanian government provides HPV vaccine for 14-years old girls for free since April 2018 (Umesikia Kuba semrikali inatoka chango kuhusu shingo ya kizazi tangu 2018) / Unajua kwamba serikali ya Tanzania inatoa chanjo ya saratani ya shingo ya kizazi kwa wasichana wenye umri kati ya miaka 14 bure kuanzia Aprili 2018?	Yes	No	DK
29.	Would you send your daughter for HPV vaccination? (Lini utampeleka mtoto kupaka dawa ya kinga ya saratani ya shingo ya kizazi) /Unaweza mwanao wa kike kupata chanjo ya saratani ya shingo ya kizazi?	Yes	No	DK
30.	Is cancer in children a problem in your community? (e.g.child with swelling tumor, lump) (Saratani ya watoto ni tatizo kwenye jamii unayoishi?) (Watoto wenye uvimbe)	Yes	No	DK
31.	Where did you use to go if something was wrong with you? (Ukipatwa na tatizo huwa unaenda wapi?)	1= Traditional healer (Mganga wa jadi) 3 =Dispensary (Zahanati) 4= Community health worker (Muhudumu wa afya) 5= Others_(Penginepo)___________		
32.	Have you ever used alcohol? (Ushawahi kutumia kikevi chochote?)/ Umeishawahi kutumia pombe?	Yes	No	
33.	Do you currently drink alcohol? (How often?) (Je, unatumia kilevi chochote kwa sasa?) Mara ngapi?	Daily: ____________________ Weekly____________		
34.	Have you ever smoked cigarettes? (Ushawahi kuvuta sigara?)	Yes	No	

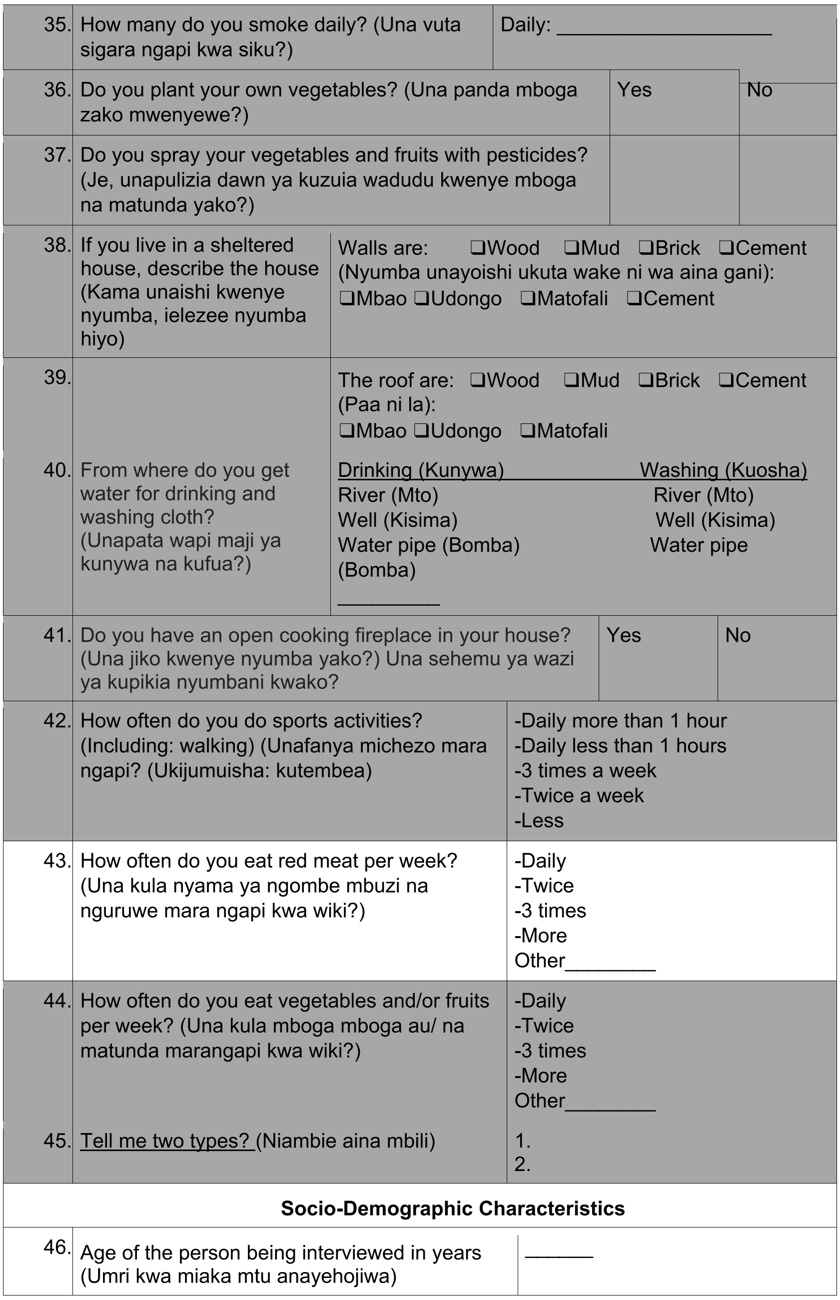
Figure 2. (Continued).

Knowledge on HPV

635 (29%) were knowledgeable about HPV. 1,644 (75%) had never heard about HPV infection. 1,118 (51%) did not know that girls can be vaccinated against cervical cancer (Figure 2). The following factors were found to have a significant impact on knowledge of HPV: Women with primary education and above, being employed, had income between 100 USD and 250 USD/month, had health insurance, and screened for cervical cancer before (Figure 5). The number of children had no association with HPV knowledge (Table 3). Women living in urban areas had less knowledge about HPV compared to rural women (Table 2).

VIA screening outcome

2,246 (80%) from 2,807 female PrevACamps attendees enrolled voluntarily for VIA-screening. 26 women were excluded from VIA because they were under 18 years of age (22), pregnancy (1), menstruation (2) and history of TAH (1). A total of 2,224 women were screened (urban: 1,039, rural: 1,185). The number of HIV infected women was 57 (2.6%). The overall mean age group was between 35 and 44 years. Among these, the proportion of positive VIA was 69 (3.1%) (Urban: 32, rural: 37, p-value = >0.478). 36 underwent cryotherapy, and 33 were referred to KCMC for LEEP or further investigations/diagnosis (Figure 1).



35.	How many do you smoke daily? (Una vuta sigara ngapi kwa siku?)	Daily: ________________	
36.	Do you plant your own vegetables? (Una panda mboga zako mwenyewe?)	Yes	No
37.	Do you spray your vegetables and fruits with pesticides? (Je, unapulizia dawn ya kuzuia wadudu kwenye mboga na matunda yako?)		
38.	If you live in a sheltered house, describe the house (Kama unaishi kwenye nyumba, ielezee nyumba hiyo)	Walls are: ☐Wood ☐Mud ☐Brick ☐Cement (Nyumba unayoishi ukuta wake ni wa aina gani): ☐Mbao ☐Udongo ☐Matofali ☐Cement	
39.		The roof are: ☐Wood ☐Mud ☐Brick ☐Cement (Paa ni la): ☐Mbao ☐Udongo ☐Matofali	
40.	From where do you get water for drinking and washing cloth? (Unapata wapi maji ya kunywa na kufua?)	Drinking (Kunywa) River (Mto) Well (Kisima) Water pipe (Bomba) (Bomba) ________	Washing (Kuosha) River (Mto) Well (Kisima) Water pipe
41.	Do you have an open cooking fireplace in your house? (Una jiko kwenye nyumba yako?) Una sehemu ya wazi ya kupikia nyumbani kwako?	Yes	No
42.	How often do you do sports activities? (Including: walking) (Unafanya michezo mara ngapi? (Ukijumuisha: kutembea)	-Daily more than 1 hour -Daily less than 1 hours -3 times a week -Twice a week -Less	
43.	How often do you eat red meat per week? (Una kula nyama ya ngombe mbuzi na nguruwe mara ngapi kwa wiki?)	-Daily -Twice -3 times -More Other________	
44.	How often do you eat vegetables and/or fruits per week? (Una kula mboga mboga au/ na matunda marangapi kwa wiki?)	-Daily -Twice -3 times -More Other________	
45.	Tell me two types? (Niambie aina mbili)	1. 2.	
	Socio-Demographic Characteristics		
46.	Age of the person being interviewed in years (Umri kwa miaka mtu anayehojiwa)	______	

Figure 2. (Continued).

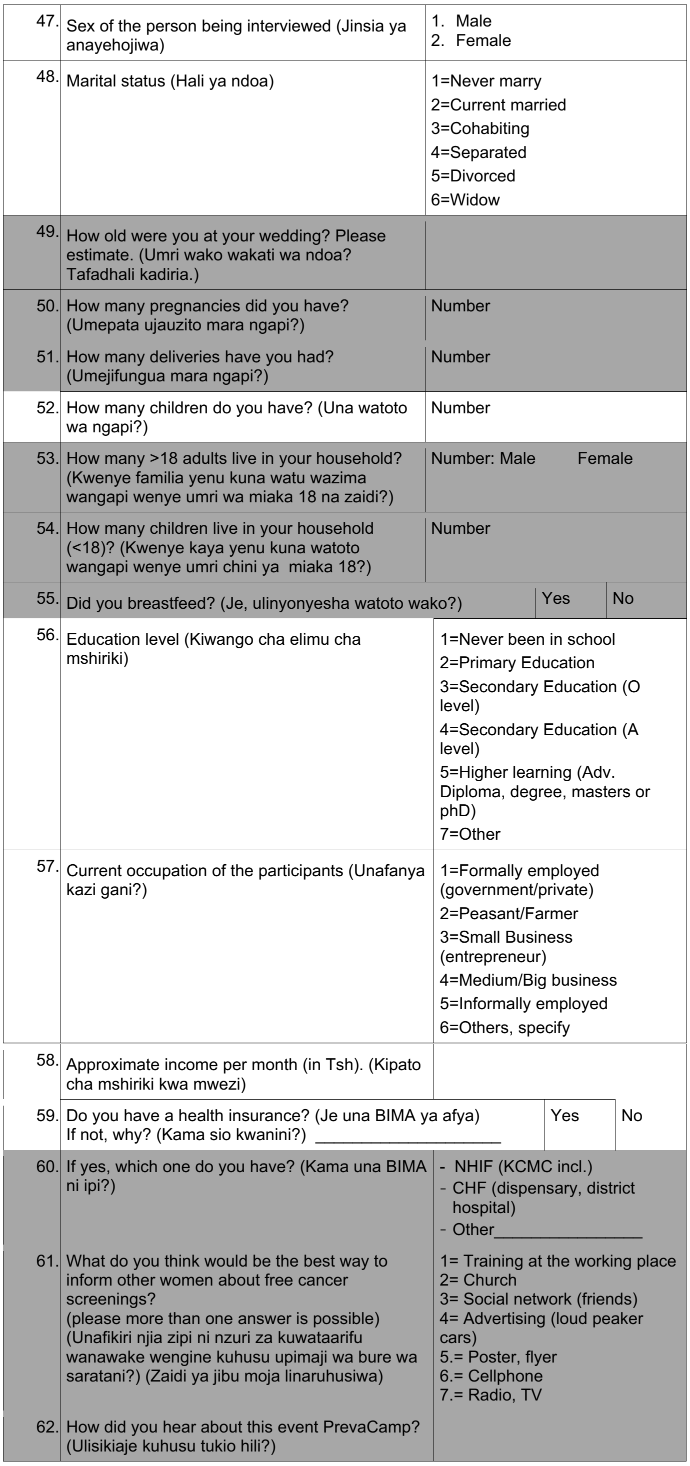
Discussion

This study accompanied PrevACamp in its real-world setting with the aim to gain a deeper understanding of cervical cancer and HPV knowledge among women attending a voluntarily screening program for future adaptations of preventive measures. The second goal of this study was to determine the prevalence of pre-cancerous cervical lesions among the attendees to identify possible regions or high-risk populations.

Our finding highlight (1) nescience on cervical cancer regardless of education level, resident status and the number of children, (2) nescience on HPV in all age groups and especially in urban areas (3) and misconception about cancer.

Cervical cancer and HPV knowledge

A third of the interviewees had never heard about cervical cancer. This compares to previous studies in Tanzania, such as a Kilimanjaro-region-based study (in semi-rural and urban areas), a study from Lake Zone and a representative country-wide survey. These studies found only 17%, 16.9% and 15% of women respectively had never heard of cervical cancer disease [7,22,27]. Our findings also show no significant difference in cervical cancer knowledge between women living in urban or rural areas as has been found in other studies [14,21,22,28]. In addition, our results demonstrate that only 22% and 29% of women showed knowledge about cervical cancer and HPV, respectively.



47.	Sex of the person being interviewed (Jinsia ya anayehojiwa)	1. Male 2. Female
48.	Marital status (Hali ya ndoa)	1=Never marry 2=Current married 3=Cohabiting 4=Separated 5=Divorced 6=Widow
49.	How old were you at your wedding? Please estimate. (Umri wako wakati wa ndoa? Tafadhali kadiria.)	
50.	How many pregnancies did you have? (Umepata ujauzito mara ngapi?)	Number
51.	How many deliveries have you had? (Umejifungua mara ngapi?)	Number
52.	How many children do you have? (Una watoto wa ngapi?)	Number
53.	How many >18 adults live in your household? (Kwenye familia yenu kuna watu wazima wangapi wenye umri wa miaka 18 na zaidi?)	Number: Male Female
54.	How many children live in your household (<18)? (Kwenye kaya yenu kuna watoto wangapi wenye umri chini ya miaka 18?)	Number
55.	Did you breastfeed? (Je, ulinyonyesha watoto wako?)	Yes No
56.	Education level (Kiwango cha elimu cha mshiriki)	1=Never been in school 2=Primary Education 3=Secondary Education (O level) 4=Secondary Education (A level) 5=Higher learning (Adv. Diploma, degree, masters or phD) 7=Other
57.	Current occupation of the participants (Unafanya kazi gani?)	1=Formally employed (government/private) 2=Peasant/Farmer 3=Small Business (entrepreneur) 4=Medium/Big business 5=Informally employed 6=Others, specify
58.	Approximate income per month (in Tsh). (Kipato cha mshiriki kwa mwezi)	
59.	Do you have a health insurance? (Je una BIMA ya afya) If not, why? (Kama sio kwanini?) ___________________	Yes No
60.	If yes, which one do you have? (Kama una BIMA ni ipi?)	- NHIF (KCMC incl.) - CHF (dispensary, district hospital) - Other________________
61.	What do you think would be the best way to inform other women about free cancer screenings? (please more than one answer is possible) (Unafikiri njia zipi ni nzuri za kuwataarifu wanawake wengine kuhusu upimaji wa bure wa saratani?) (Zaidi ya jibu moja linaruhusiwa)	1= Training at the working place 2= Church 3= Social network (friends) 4= Advertising (loud peaker cars) 5.= Poster, flyer 6.= Cellphone 7.= Radio, TV
62.	How did you hear about this event PrevaCamp? (Ulisikiaje kuhusu tukio hili?)	

DK: don´t know, The questions highlighted in grey were not analyzed in this study

Figure 2. (Continued).

These findings are in line with studies from other SSA settings [7,18,22,27,29–31].

Surprisingly, women living in urban areas had less knowledge about HPV compared to rural women (Table 2), which might be carefully interpreted by the presence of many faith-based hospitals, NGO´s and other health facilities [32] in rural Kilimanjaro, which is unique for Tanzanian rural areas.

Apart from the afore mentioned, we found significant differences in the level of cervical cancer knowledge in our study population. Women with higher income, health insurance, and previous experience of VIA screening had significantly more knowledge about cervical cancer. This is possible because women who have health insurance may have better health-seeking behavior and have had more interaction with health facilities. These findings are in tandem with results from a study from Zanzibar [30]. Another study from Zimbabwe found that women with a higher income, and who had more contact with the health care system had better cervical cancer knowledge [29].

Table 1. Overview about PrevACamp attendees.

No	Regions	Districts	Sites	Number of attendees	Interviewees (%)	HIV infected women	VIA screened women	VIA positivity (%)	Cryo-therapy	Referral for LEEP to KCMC	Health Insurance (%)
1.	**Kilimanjaro**	Moshi urban	Moshi Urban	1081	916(42)	23	875	30(3,4)	16	14	**422(46)**
2.		Hai	Machame	252	185(8)	2	20	5(2,5)	3	2	**103(56)**
3.		Moshi rural	TPC	125	116(5)	4	125	3(2,4)	0	3	**45(39)**
4.		Siha District	Sanya Juu	232	165(8)	3	178	5(2,8)	4	1	**40(24)**
5.		Moshi rural	Mahoma	381	248(11)	10	249	11(4,4)	5	6	**67(27)**
6.		Rombo	Huruma (Rombo)	335	284(13)	3	255	7(2,7)	6	1	**154(54)**
7.		Neema (Mwanga)	Mwanga	187	120(6)	6	176	6(3,5)	0	6	**55(46)**
8.	**Arusha**	Arusha urban	Arusha urban	214	158(7)	6	164	2(1,2)	2	0	**76(48)**
	Total			**2,807**	**2,192(78)**	**57**	**2,224**	**69(3,1)**	**36**	**33**	**962(44)**

KCMC = Kilimanjaro Christian Medical Centre, VIA = Visual inspection using acetic acid, LEEP = Loop Electrosurgical Excision Procedure.

Education level and employment appear to play no role in the knowledge about cervical cancer in our study. These results are not consistent with other studies in SSA [7,22,30,31]. Also, no correlation was found between multiparous and cervical cancer knowledge, as has been reported in previous studies from Tanzania [22,32]. However, a study from India documented that a high number of pregnancies, using family planning, and frequent contact with the health-care system found to be associated with increased access of cervical cancer screening services [33]. A possible explanation for the differences in our study with previous studies could be that our study population was not a representative sample or a hospital patient population, which can be assumed to have higher health-seeking behavior. Following this line of reasoning, the PrevACamps reached people with less than average knowledge and hence the desired target group for an intervention program was addressed.

A second explanation could be the timing of the previously conducted studies: the NCCS by MoHSW was introduced in 2013 [15,22]. In the years before and after NCCS implementation (mainly in the years of 2012 to 2015), cervical cancer and screening programs received great nationwide attention through mass media [22] and increased governmental support, especially from the former First Lady Her Excellency Salma Kikwete [34,35].

Following the logic of influences in mass media and government engagement, we consequently see higher knowledge regarding HPV vaccination compared to Cervical Cancer knowledge in our study population. During the PrevACamps, HPV vaccination implementation campaigns in schools were conducted country-wide [16,17], and announcements through mass media were frequently given.

Misconception about cancer

Another major barrier to combat cancer is the misconception about cancer. Our study found that every second woman living in rural areas has misconceptions about cancer which may lead to disbelief and heedlessness toward cancer prevention [19,36]. The influence of sociocultural beliefs in relation to cervical cancer misconceptions has been studied before but with inconsistent findings. McCree et al. found key stakeholders in Tanzania believed that the perception of low resources was a stronger barrier than the impact of folk myths and sociocultural-based misconceptions [34]. This is contradicted with Zambia's report where folk myths and misconceptions lead to poor utilization in cancer education and screening services [37]. Cervical cancer may impact HIV infected women differently than other populations. Studies show that women infected with

Table 2. Behavioral risk factors, women's knowledge about cancer, cancer risk factors, cervical cancer and HPV by residence.

Variables	Total N (%)	Urban N (%)	Rural N (%)	OR (95%CI)	p-value
Behavioral Risk Factors					
Cigarette Smoking	Total	Urban	Rural		
No	**2,136(97.4)**	543(97.1)	1,593(97.6		
Yes	**56(2.6)**	16(2.9)	40(2.4)	1.17(0.65–2.11)	0.593
Alcohol use					
No	**1,174(53.6)**	300(97.1)	874(97.6)		
Yes	**1,018(46.4)**	259(2.9)	759(2.4	0.99(0.82–1.21)	0.952
Red meat intake weekly					
Less/none	**1,742(79.5)**	422(75.5)	1,320(80.8)		
More/daily	**450(20.5)**	137(24.5)	313(19.2)	**1.39(1.09–1.72)**	**<0.0070**
Knowledge about cancer					
Household members with cancer currently	Total	Urban	Rural		
No	**1887(86.1)**	488(87.3)	1,399(85.7)		
Yes	**305(13.9)**	71(12.7)	234(14.3)	0.87(0.65–1.16)	0.337
History of household members with cancer					
No	**1,594(72.7)**	380(68.0)	1,214(74.3)		
Yes	**598(27.3**	179(32.0)	419(25.7)	**1.36(1.11–1.68)**	**<0.004**
Cancer problem in the community					
No	**1,041(47.5)**	275(49.2)	766(46.9)		
Yes	**1,151(52.5)**	284(50.8)	867(53.1)	0.91(075–1.11)	0.350
Heard about cancer before					
No	**407(18.6)**	74(13.2)	333(20.4)		
Yes	**1,785(81.4)**	485(86.8)	1,300(79.6)	**1.68(1.28–2.21)**	**<0.0002**
Misconceptions in getting cancer	Multiple answers	N = 164	N = 781		
Curse	**115(12.3)**	10(6.1)	105(13.6)	**2.39(1.22–4.70)**	**<0.0089**
Genetic mutation	**403(43.1)**	88(53.7)	315(40.9)	**0.58(0.42–0.82)**	**<0.0017**
Direct contact	26(**2.8)**	5(3.0)	21(2.7)	0.88(0.33–2.37)	0.7979
Vaccine	**54(5.8)**	2(1.2)	52(6.7)	**5.78(1.38–24.12)**	**<0.0064**
Contraceptive use	**288(20.4)**	37(22.6)	251(32.6)	**1.63(1.09–2.42)**	**<0.0155**
Knowledge about cervical cancer					
Knowledge about CC	Total	Urban	Rural		
Poor	**1,708(77.9)**	430(76.9)	1,278(78.3)		
Good	**484(22.1)**	129(23.1)	355(21.7)	1.08(0.86–1.36)	0.510
Heard about CC prior PrevACamp					
No	**731(33.3)**	178(31.8)	553(33.9)		
Yes	**1,461(66.7)**	381(68.2)	1,080(66.1)	1.07(0.87–1.32)	0.5093
Screened for CC prior PrevACamp					
No	**1,942(88.6)**	468(83.7)	1,474(90.3)		
Yes	**250(11.4)**	91(16.3)	159(9.7)	**1.80(1.36–2.38)**	**<0.0001**
Risk factors for CC					
Not aware	**2009(91.7)**	521(93.2)	1,488(91.1)		
Aware	**183(8.3)**	38(6.8)	145(8.9)	**0.75(0.52–1.08)**	**<0.1247**
Lower risk for CC					
Not aware	**2057(93.8)**	526(94.1)	1,531(93.8)		
Aware	**135(6.2)**	33(5.9)	102(6.2)	**0.94(0.63–1.41)**	**<0.7711**
Symptoms about CC					
Not aware	**1,671(76.2)**	424(75.8)	1,247(76.4)	ref	
Aware	**521(23.8)**	135(24.2)	386(23.6)	1.03(0.82–1.29)	0.8058
Vaginal bleeding after menopause is a sign of CC					
Not aware	**1174(53.6)**	299(53.5)	875(53.6)	ref	
Aware	**1,018(46.4)**	260(46.5)	758(46.4)	1.01(0.83–1.22)	0.9693
Knowledge of Human Papillomavirus					
Heard about HPV infection	Total	Urban	Rural		
Not aware	**1,693(77.2)**	433(77.5)	1,26,077.2)		
Aware	**499(22.8)**	126(22.5)	373(22.8)	0.98(0.78–1.24)	0.8835
Heard about HPV vaccines					
Not aware	**1,175(53.6)**	316(56.5)	859(52.6)		
Aware	**1,017(46.4)**	243(43.5)	774(47.4)	0.85(0.70–1.04)	01082
Knowledge about HPV					
Poor	**1,548(70.6)**	414(74.1)	1,134(69.4)		
Good	**644(29.4)**	145(25.9)	499(30.6)	**0.8.(0.64–0.99)**	**<0.039**

CC = Cervical Cancer, HPV = Human Papillomavirus, PrevACamp = Cancer and Awareness Campaign.

HIV are more likely to appear with cervical cancer disease later in life [38,39]. Bateman et al. assessed barriers to cervical cancer screening among HIV infected women in Tanzania and found that women had high misconceptions of cervical cancer screening and felt that diagnosis may lead to death, hence hindering women from seeking health care [39].

Need for extended cancer education and screening programs

PrevACamp was the first community-based prevention and awareness cancer campaign organized by CCC in Northern Tanzania. The framework combined cancer education seminars and screenings for women, especially in remote areas.

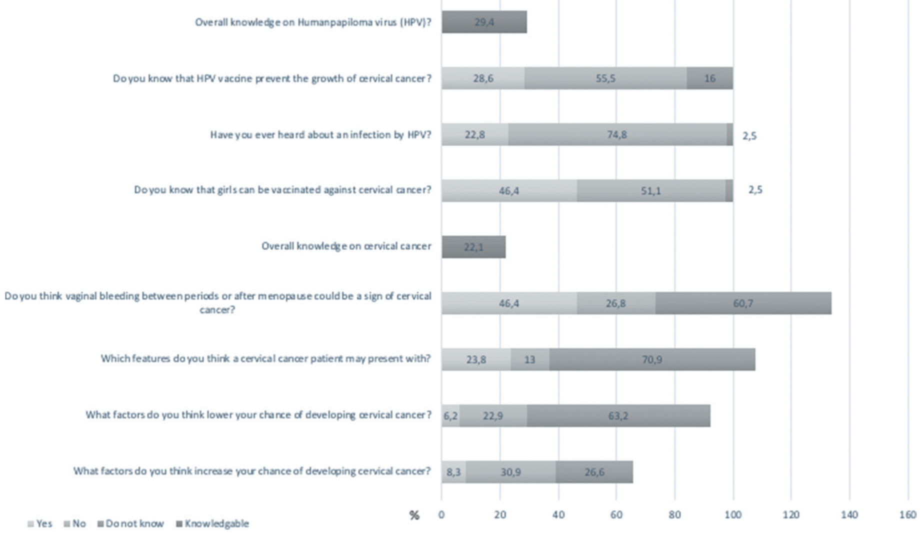


Figure 3. Knowledge level of cervical cancer and HPV.

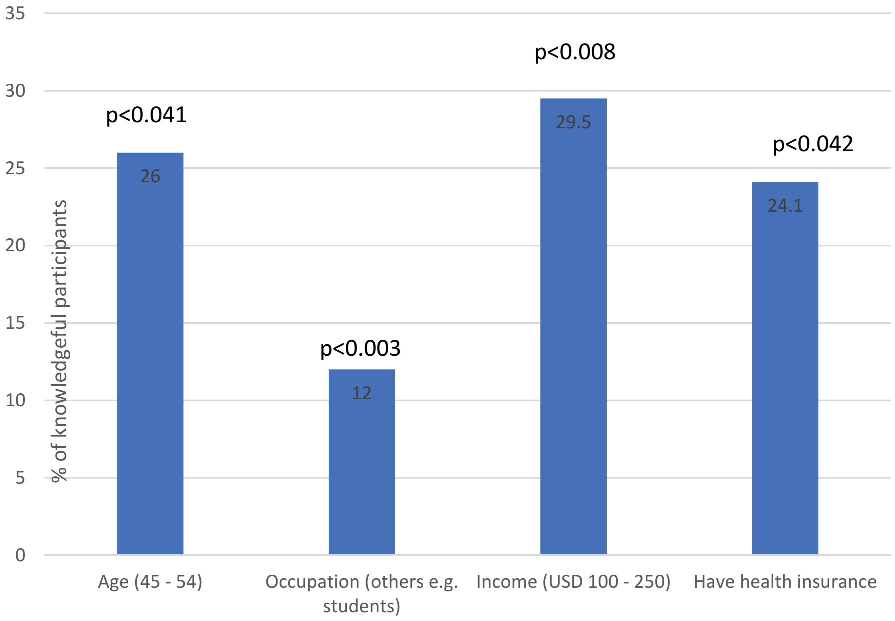


Figure 4. Association between social demographic characteristics and Cervical Cancer knowledge.

Considering 75% of reproductive-aged women live in rural areas [28], outreach programs covering these areas are crucial [21,40], especially as higher rates of family history of cancer were reported in rural areas. Our study found that 76% of women residing in rural areas were not able to identify any early symptoms, risks, or preventive factors of cancer. Apart from this, previous studies have shown that access to health care differs between women in rural and urban areas, largely due to transportation and financial constraints that prevent screening attendance [21,40,41]. Therefore, enhancement of cancer knowledge, that is needed to increase women's health, might be best achieved by bringing screening and education into the rural areas.

Comparatively, in a review from Runge et al. with a cumulative VIA positivity rate of 9.2%, our VIA positivity rate was 3.1% [14]. However, the reviewed studies showed vast difference with VIA positive screening results ranging from 4.3% (with the study setting in Dar es Salaam, in Dar es Salaam/Pwani and Mwanza/Mtwara) to 12.9% (in Mwanza/Mara). Just like prior PrevACamps, the VIA screening programs targeted the general population and were announced in public [14]. The differences with low VIA positive screening results could be explained by the high density in primary health care facilities including HIV clinics in these settings [32]. This might also influence the lower VIA positivity in our study with only 2.6% of HIV infected participants, compared with the study from Mara where 8.2% were infected with HIV [38]. Furthermore, PrevACamp findings showed no significant difference between residence status and VIA-positivity. Following

Table 3. Association between sociodemographic characteristics and cervical cancer/HPV knowledge.

	Total	Knowledge of CC			Knowledge of HPV		
Variables	N	N(%)	OR(95%CI)	p-value	N(%)	OR(95%CI)	p-value
Age, years							
<25	194	36(18.6)	1.00		52(26.8)	1.00	
25–34	460	110(23.9)	1.38(0.91–2.10)	0.134	152(33.0)	1.35(0.93–1.96)	0.116
35–44	571	122(21.4)	1.19(0.79–1.80)	0.404	181(31.7)	1.27(0.88–1.82)	0.201
45–54	469	122(26.0)	**1.54(1.02–2.34)**	**<0.041**	151(32.2)	1.30(0.89–1.88)	0.171
55+	498	94(18.9)	1.02(0.67–1.56)	0.923	108(21.7)	0.76(0.52–1.11)	0.152
Education level							
Never been in school	131	28(21.4)	1.00		19(14.5)	1.00	
Primary education	1430	289(20.2)	0.93(0.60–1.44)	0.751	382(26.7)	**2.15(1.30–3.54)**	**<0.003**
Secondary and above	631	167(26.5)	1.32(0.84–2.08)	0.225	243(38.5)	**3.69(2.21–6.16)**	**<0.0001**
Occupation							
Peasant/farmer	944	207(21.9)	1.00		261(27.6)	1.00	
Business	542	120(22.1)	1.01(0.78)	0.924	156(28.8)	1.06(0.83–1.34)	0.640
Employed	523	135(25.8)	1.24(0.97–1.59)	0.092	182(34.8)	**1.40(1.11–1.76)**	**<0.004**
Other e.g. students	183	22(12.0)	**0.49(0.30–0.78)**	**<0.003**	45(24.6)	0.85(0.59–1.23)	0.395
Level of income (USD $)							
<50	1295	277(21.4)	1.00		353(27.3)	1.00	
50-<100	394	76(19.3)	0.88(0.66–1.17)	0.369	102(25.9)	0.93(0.72–1.20)	0.591
100–250	220	65(29.5)	**1.54(1.12–2.12)**	**<0.008**	85(38.6)	**1.68(1.25–2.26)**	**<0.001**
>250	109	32(29.4)	1.53(0.99–2.36)	0.055	45(41.3)	**1.88(1.26–2.80)**	**<0.002**
Unknown	174	34(19.5)	0.89(0.60–1.33)	0.575	59(33.9)	1.37(0.98–1.92)	0.068
Health Insurance							
Yes	962	232(24.1))	**1.23(1.01–1.51)**	**<0.042**	310(32.2)	**1.28(1.06–1.53)**	**<0.010**
No	1230	252(20.5)	1.00		334(27.2)	1.00	
Residence							
Urban	559	129(23.1)	1.08(0.86–1.36)	0.510	145(25.9)	0.80(0.64–0.99)	**<0.039**
Rural	1633	355(21.7)	1.00		499(30.6)	1.00	
Children							
No	215	39(18.1)	1.00		68(31.6)	1.00	
Yes	1977	445(22.5)	1.31(0.91–1.88)	0.4143	576(29.1)	0.89(0.66–1.20)	0.446
Ever screened for CC							
No	1942	399(20.5)	1.00		546(28.1)	1.00	
Yes	250	85(34.0)	**1.99(1.50–2.65)**	**<0.0001**	98(39.2)	**1.65(1.26–2.16)**	**<0.0001**

CC = Cervical Cancer, HPV = Human Papillomavirus.

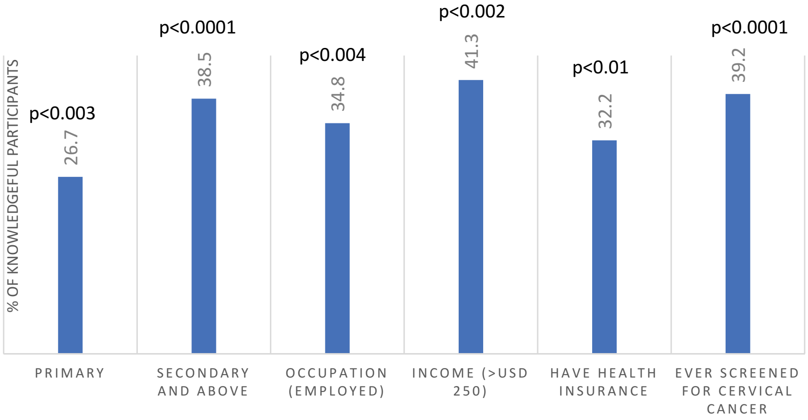


Figure 5. Association between social characteristics and HPV knowledge.

this line, the setting in our study has the highest density of primary health care facilities after Dar es Salaam and also a long-standing tradition of faith-based hospitals [42]. The health system coverage in our setting may as well be a positive impact on HIV patients and influence the lower VIA positivity rate.

Limitations

Study findings cannot be generalized for the Tanzanian population as our sample represents voluntarily attending women from Northern Tanzania. During VIA screening, women above the age of 18 years were enrolled. However, WHO guidelines recommend screening at age 30 years old onwards. This might have also contributed to a lower positive VIA screening outcome.

Conclusion

Our findings show a lack of cervical cancer and HPV knowledge among women in two regions in northern Tanzania. This poor knowledge is alarming and requires collaborative efforts from different stakeholders including health care providers, policymakers, and non-governmental organizations to increase cancer knowledge within the communities. Education-based cancer knowledge programs and mass screening programs, especially in remote areas should be considered, as this approach will reach the underserved rural population. Future cancer programs that strengthen the collaboration with public schools for primary and secondary prevention and to extend special cancer education programs on mass media and loudspeaker cars should also be considered.

Educational program to raise knowledge about HIV infections in the community is also needed to reach a standard level of knowledge and understanding about the importance of HIV prevention, treatment and cervical cancer screening. Another step would be to set up more cervical cancer screening centers in the primary health care in remote areas, collaboration of multiple stakeholders such as cancer survivors and community health care workers are essential with sufficient screening equipment's. Provided, cancer care staff workloads do not increase, added funds for health care providers for cancer awareness training are required [17].

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Author contributions

All authors contributed to the overall concept of the paper. AH and OH wrote the draft that was improved by editing from all authors. Funding acquisition, conceptualization of the project and formal analysis were performed by AH. Data collection were done by BM and FS. Methodology and interpretation of the data were done by AH, OH, UK, TB. Writing review and the final approval of the version to be published was done by AH and OH.

Disclosure statement

All authors declare no financial or any other conflicts of interest.

Ethics and consent

Ethical research clearance was secured from Kilimanjaro Christian Medical University College in Moshi, Tanzania.

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Paper context

14.9 million women in Tanzania are at risk of developing cervical cancer, the most prevalent cancer among women in this East African country. Late-stage presentation contributes to high mortality rates. Between 2017 and 2019, a study was conducted amongst 2,807 female participants of prevention and awareness campaigns in northern Tanzania. Results display significant nescience on cervical cancer and HPV. Outreach programs, especially in rural areas, seem to target the population in need of health education.

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Singer R, Henke A, Alloyce JP, Serventi F, Massawe A, **Henke O.** (2019) Repetitive Cancer Training for Community Health Care Workers: An Effective Method to Strengthen Knowledge and Impact on the Communities. Results from a Pilot Training at Kilimanjaro Region, Tanzania. J Cancer Educ, 36(3), 470-47

Zielsetzung der Arbeit: Es sollte aufgezeigt werden, ob kurze und repetitive Interventionstrainings bei Gesundheitsarbeiterinnen und -arbeitern auf Gemeindeebene (Community Health Workers (CHW) und Dispensary Health Workers (DHCW)) das Wissen um Krebs und die Einbindung in die tägliche Routinearbeit mit der Bevölkerung verbessern können.

Methoden und Ergebnisse: Ein Mixed-Method Approach wurde angewendet, mit Pre- und Posttests (Multiple Choice (MC) und eine offene Frage) vor und nach den Trainingseinheiten. Nach Abschluss aller Trainingseinheiten wurden Fokusgruppen-Diskussionen (FGD) in Kleingruppen durchgeführt. Die MC-Fragen wurden deskriptiv mit univariaten Häufigkeiten ausgewertet, die qualitativen Daten mittels Inhaltsanalyse. Insgesamt nahmen 41 in ländlichen Gegenden registrierte CHW und DHCW an den Trainings und den Tests teil. Die Ergebnisse zeigten einen signifikanten Anstieg des Wissens um Krebserkrankungen in beiden Gruppen jeweils nach den Trainings und nach drei Monaten. Kategorien der FGD-Auswertung waren: „Educating and advising people“, „Building self-confidence and knowledge”, “Misbeliefs and alternative medicine” und “Building networks”.

Schlussfolgerungen: Kurzinterventionen mit repetitiven Ein-Tages-Trainings sind effektiv, um Krebswissen unter CHW und DHCW deutlich zu verbessern. Zudem fördern die Trainings das Selbstbewusstsein und die Sicherheit im Umgang mit Patientinnen und Patienten und der Bevölkerung. Vor dem Hintergrund des Mangels an spezialisierten Gesundheitsarbeiterinnen in Tansania, kommen den CHW/DHCW eine große Bedeutung auch in der Gesundheitsaufklärung der Bevölkerung zu und können diese dazu beitragen die rasch steigende Krebsinzidenz zu adressieren.

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Repetitive Cancer Training for Community Healthcare Workers: an Effective Method to Strengthen Knowledge and Impact on the Communities: Results from a Pilot Training at Kilimanjaro Region, Tanzania

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Abstract

Cancer is a growing burden in Tanzania with high mortality rates. Low level of cancer awareness in the population and health workforce is one of the reasons. This study aimed to evaluate the effects of a cancer awareness training for community-level healthcare providers in Kilimanjaro Region. Main research interest was to assess the effects of the training on cancer knowledge of the healthcare workers and its application into practice. Community health workers (CHWs) ($n = 25$) and dispensary healthcare workers (DHCWs) ($n = 16$) attended cancer awareness trainings. Three training days over a 3-month period were provided for each group. Pre- and post-training assessments of the cancer knowledge were conducted on each training day. Application of the knowledge into practice was assessed at follow-up and complemented with qualitative data. Analysis of the questionnaires was provided by descriptive statistics. Qualitative data were analyzed by semantic thematic analysis. Both groups showed a statistically significant increase in knowledge after the three training days: CHWs + 10% (CI 95% = 2–18%, $p = 0.015$) and DHCWs 24.4% (CI 95% = 13–36%, $p = 0.002$). The community-level healthcare providers also started to apply the new cancer knowledge into practice and reported to feel more confident in cancer control. The pilot cancer awareness training was effective in increasing cancer knowledge and its application. It strengthened their confidence in care delivery and referral practices as well as education of the population. This concept of cancer awareness training might be also applicable to other countries in SSA.

Keywords Cancer · Tanzania · Community health workers · Prevention · Training · Education

Background

Cancer in Sub-Saharan Africa and Tanzania

The global cancer incidence is increasing [1]. In sub-Saharan Africa (SSA), the burden of cancer is estimated to increase by 85% by the year 2030 [2]. Especially in low-income countries (LICs), demographic transition and changes in lifestyle are main facilitators for this growth [1].

The highest incident cancers in Tanzania are cervical and breast cancer in women, prostate cancer in men, and Kaposi sarcoma, hepatocellular cancer, and non-Hodgkin lymphoma in all genders [1]. Many cancer entities are related to infections with viruses such as human immunodeficiency virus (HIV), hepatitis B, and human papilloma virus (HPV). The number of infection-related cancers is distinctly higher in SSA compared to other regions in the world [3].

Especially, mortality rates in many SSA countries are remaining high [1]. Countries in Eastern Africa, including Tanzania, show one of the highest cancer mortality rates in women worldwide [4]. The proportionally higher mortality and case-fatality rates of cancer in SSA have various reasons, and hence, different measures need to be taken to approach this problem. Weak health systems with barriers to access and impoverishing effects for help-seeking patients are key factors, but also less interest in cancer and other noncommunicable diseases (NCDs), due to competing health needs by communicable diseases (CDs). The biggest part of official development

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assistance and measures by governments in the SSA region are directed to control diseases with higher prevalence, like HIV/AIDS, malaria, and tuberculosis [2]. Additionally, there is a lack of a (trained) health workforce, inadequate cancer registries, as well as fear and misbeliefs in the population. Finally, this leads to relatively low levels of cancer awareness in the population and is facilitating deficient prevention measures, screening, and treatment [5]. This low awareness among the population of SSA is an important reason, contributing to the high rates of cancer mortality [5]. Patients reach hospitals and adjuvant treatment often at a late, not curable stage of cancer [6, 7]. A facilitator of this late help-seeking behavior is an additional low level of cancer awareness in many healthcare workers [8–10].

Treatment of cancer in Tanzania is available at three hospitals in the country [11]. Nevertheless, long distances to these health facilities as well as often unaffordable public transport impedes access to healthcare services for many of the rural population [12], which are about 70% of the Tanzanian population [13]. Hence, the patients in these areas often seek help from community health workers (CHWs), dispensary healthcare workers (DHCWs), or local healers. This emphasizes the importance of these community-level healthcare providers for primary healthcare. Their outreach work in the rural areas is an important and effective public health measure to link people to essential healthcare services [14].

CHWs are active at the village level. These volunteers are community members trained in basics of healthcare, prevention, and health promotion. They are para-professionals and receive a general medical training for approximately 6 weeks [15]. However, they are important to provide “culturally appropriate” health services to the community [16]. CHWs are an effective public health measure to complement the lack of a professional health workforce, increase access to healthcare services, and improve health outcomes. They are already an important resource to improve health outcomes of CDs and maternal and child health in many LMICs [14]. The CHWs participating in this study were mainly focusing on maternal and child health as well as HIV/AIDS services.

DHCWs working at the ward level ideally should have a professional background as nurses or medical assistants with medical training of 2 to 3 years. Due to a shortage of trained health workforce in Tanzania, dispensaries are often lacking these professionals with comprehensive education and their posts are taken by para-professionals as well [10, 17].

The village and ward-level healthcare workers are summarized in this paper with the term community-level healthcare providers.

Together, CHWs and DHCWs are the biggest groups of the Tanzanian health workforce and are already an important resource to improve health outcomes of CDs. But there is still a gap of addressing and assessing their knowledge of NCDs [16]. First studies in the SSA region showed that cancer knowledge of CHWs, especially about risk factors and symptoms, is low and there is a need for cancer trainings to increase their knowledge, confidence, and impact on cancer control [18].

PrevACamp and PrevATrain

To address these problems, the Prevention and Awareness Campaign (PrevACamp) was implemented in October 2017. This campaign targets citizens of the Kilimanjaro Region and is carried out by the Cancer Care Center (CCC) at the Kilimanjaro Christian Medical Centre (KCMC) in Moshi. Goals of PrevACamp are aligned with several goals of the National Cancer Control Strategy (NCCS) of Tanzania, like prevention and development of human resources [19]. One pillar of the campaign aims to improve cancer awareness in the population, promote health, and improve early detection of the disease due screening. Another pillar addresses CHWs and DHCWs, to raise their cancer awareness and improve referral of cancer patients from rural areas to CCC for further diagnosis and treatment. To achieve this aim, a training program “Prevention and Awareness Training” (PrevATrain) was developed.

Aim of the study was to examine the effects of the pilot PrevATrain. Main purpose was to assess the impact on healthcare workers’ knowledge about cancer. Secondly, it assessed how well the community-level healthcare workers could apply their new knowledge into practice.

Methods

Study Cohort and Design

A purposive sample of a group of 25 CHWs and 16 DHCWs from the Kilimanjaro Region were invited to attend PrevATrain. To be eligible for the training, the CHWs and DHCWs had to work as registered health workers in communities in rural areas in Northern Tanzania.

Pre- and post-training surveys were conducted to assess the impact on their knowledge about cancer and its application into their routine practice. The data were complemented with qualitative data. Ethical research clearance was secured from the Kilimanjaro Christian Medical College in Moshi, Tanzania.

Cancer Awareness Training

The training was structured in 3 days (1 day in three subsequent months) and were modified for the two groups to meet their respective foreknowledge.

Core content of the training was taught on the first day with a curriculum comprising cancer in general, cancer entities, symptoms, risk factors, strategies for early detection (screening), treatment, and palliative care. A special focus was on cervical and breast cancer. Additional information about the CCC and referral pathways were given. Recapitulating information were given on the second and third training days, followed by workshops to exchange experiences in small group discussions of 6–8 participants. Training and discussion were conducted in Swahili.

Survey Instruments

The questionnaire about cancer knowledge was developed as multiple choice (MC) questionnaires for the pre-/post-training comparison and was applied before and after every training. Application of the knowledge into practice was assessed with open-ended questions in the post-training surveys on training days 2 and 3 and complemented with qualitative data from observational notes during group discussions.

The MC questionnaire for the CHWs contained 16 questions and one open-ended question, and the DHCWs had 19 questions for knowledge assessment and the same open-ended question.

Analysis of the quantitative data was performed by using the software IBM SPSS Statistics Version 25 and included descriptive statistics with univariate frequency calculations. Mean scores of the MC test results provide comparison of the knowledge level before and after the trainings. Paired *t* test was used for statistical hypothesis testing. The open-ended questions and qualitative data were coded and analyzed by semantic thematic analysis. For qualitative data analysis, MAXQDA 2018 software was used.

Results

The results display a significant increase in cancer knowledge in both groups in the 3-month follow-up. Besides the increase in knowledge, the community-level healthcare providers started to apply the new knowledge successfully into their work.

Eight out of 16 DHCWs and 15 out of 25 CHWs participated in all three training sessions and in all four assessments. The sociodemographic data of the participants are shown in Table 1.

Table 1 Sociodemographic characteristics, baseline samples, CHWs (*n* = 25) and DHCWs (*n* = 16)

Variable	CHWs, no. (%)	DHCWs, no. (%)
District		
Hai	0 (0)	1 (9.1)
Moshi rural	20 (80)	7 (63.6)
Moshi urban	1 (4)	1 (9.1)
Simanjiro	4 (16)	2 (18.2)
Gender		
Female	18 (72)	10 (90.9)
Male	6 (24)	1 (9.1)
Missing	1 (4)	0 (0)
Age (years)		
18–29	5 (20)	2 (18.2)
30–39	2 (8)	1 (9.1)
40–49	6 (24)	2 (18.2)
50–59	8 (32)	4 (36.4)
60–69	1 (4)	1 (9.1)
70 above	1 (4)	0 (0)
Missing	2 (8)	1 (9.1)
Education		
Primary school	16 (64)	5 (45.5)
Secondary school	4 (16)	5 (45.5)
University	5 (20)	1 (9.1)
Occupation		
Farmer	15 (60)	0 (0)
Formal employed (govt/private)	4 (16)	11 (100)
Informal employed/entrepreneur	4 (16)	0 (0)
Missing	2 (8)	0 (0)
Duration of working as a CHW/DHCW		
Less than 1 year	3 (12)	0 (0)
1–5 years	5 (20)	3 (27.3)
More than 5 years	17 (68)	8 (72.7)
Previous cancer education/training		
No	25 (100)	10 (90.1)
Yes	0 (0)	1 (9.1)
Ever cared for people with cancer		
Yes	13 (52)	3 (27.3)
No	7 (28)	7 (63.6)
Missing	5 (20)	1 (9.1)

CHW community health worker, *DHCW* dispensary healthcare worker

Results for Community Health Workers

CHWs had an increase in their cancer knowledge of 10% from a good to a very good knowledge level. Already after the first training, an increase of their knowledge has been shown. After repeating the curriculum, exchange of experience and group work discussions in the second and third training days, their knowledge increased further, especially after the third training, where it reached the highest score (Table 2). The score after the second training was lower than after the first but still showed an increase when compared to the baseline score.

The CHWs' cancer knowledge showed distinct growth in the different topics of the training. Topics with a high baseline knowledge level showed minimal increase over the training period, e.g., basic knowledge about palliative care and referral

Table 2 Scores in pre- and post-training cancer knowledge assessment, CHWs, follow-up sample ($n = 15$)

	Mean[1]	Std. deviation	Percentage of total score	Paired samples *t* test sig. (2-tailed)
Baseline score	11.7	1.831	65%	
Post I score	13.3	2.549	74%	
Post II score	12.6	1.404	70%	
Post III score	13.6	2.530	76%	
Range post III score—baseline			10%	0.015

[1] Total score of 18; knowledge level: 18–14 = very good, 13–9 = good, 8–4 = fair, 3–0 = poor

pathways. Other topics, like cancer incidence in Tanzania, cervical cancer, its risk factor HPV, and prevention measures, showed higher increase.

The qualitative data analysis displayed a high motivation to put their new knowledge into practice. The participants expressed how they educate the communities about cancer and talk about the importance of its early detection and prevention. They also reported to have encouraged people to stop going to their local healers for cancer treatment. Furthermore, it was stated that the confidence in conducting their work of cancer control was strengthened. Talking to their communities about cancer to reduce misbelief and to advise women to go for cervical cancer screening were the most common topics in their interaction with the community. CHWs started networking with other health facilities and referred 18 patients with suspected cancer diagnosis directly to the Cancer Care Centre at KCMC within 6 months after the training. Four categories were identified and displayed in Table 3.

Results for Dispensary Healthcare Workers

The increase in cancer knowledge among the DHCWs reached 24%, from good knowledge to very good knowledge after all three trainings. Their knowledge increased steadily after each training (Table 4).

Different topics showed different knowledge growth during the trainings. In topics like pathophysiology of cancer, cervical cancer risk factor HPV, and the referral pathway, they already had a good knowledge level before the training and showed little impact. Other topics, like breast examination, staging investigations, and side effects of chemotherapy, showed stronger effects from poor to good knowledge levels.

Besides the increase of their cancer knowledge, the qualitative data showed that DHCWs became more confident and motivated to educate their communities and coworkers about cancer, its risk factors, screening, treatment, and importance of early detection. Some already started to implement cervical and breast cancer screenings in their dispensary work. They also reported to feel more confident about the referral pathway and started to network with other health facilities to provide outreach cancer screening in the communities. Additionally, they were more confident to counsel about the impact of cancer treatment with local herbs (provided by local healers) and modern medicine (Table 4).

Training Effect on CHWs and DHCWs Compared

Both groups had a significant increase in their cancer knowledge. Overall, the CHWs had 11% (95% CI = 2–18%, $p = 0.015$) more cancer knowledge after all three training sessions, and the DHCWs gained 24% (95% CI = 13–36%, $p = 0.002$) more knowledge (Fig. 1).

In some selected questions, such as cancer incidence in Tanzania and transmission of HPV, both groups had a similar pre-test knowledge and a similar growth after the trainings. Regarding the overall cancer knowledge in the comparable pre-test questions and increase after completing the training period, no remarkable difference between the groups can be observed (Fig. 2).

Table 3 Scores in pre- and post-training cancer knowledge assessment, DHCWs, follow-up sample ($n = 8$)

	Mean[1]	Std. deviation	Percentage of total score	Paired samples *t* test sig. (2-tailed)
Baseline score	11.1	3.871	53%	
Post I score	12.6	2.560	60%	
Post II score	14.4	2.615	69%	
Post III score	16.3	1.832	77%	
Range post III score—baseline			24%	0.002

[1] Total score of 21; knowledge level: 21–16 = very good, 15–10 = good, 9–5 = fair, 4–0 = poor

Table 4 Categories and themes from qualitative content analysis among participants

Category	Themes
Educating and advising people	• Education about cancer in the community by outreach, door-to-door consulting or in parishes, creating cancer awareness, e.g., how avoid risk factors advice and educate about cancer, screening and checkup, importance of early detection, prevention • Advice people to go for screening (cervical, breast and prostate) and treatment to health facilities • Consultation and education of coworkers, act as multipliers
Building self-confidence and knowledge	• More confidence in consulting women about cancer • Motivation to continue in learning about cancer • Support and care for cancer patients and palliative patients in the community • Referral to regional hospital due to sensitization for cancer • More confident in distinguishing between breast cancer and other breast issues/disease • More confident in provision of screening for cervical and breast cancer and integration into outpatient services
Misbeliefs and alternative medicine	• Talk with people about cancer treatment by local healers and stop them to go there • Reduce misbeliefs about cancer e.g. that it is not a contagious disease; cancer is curable if early detected
Building networks	• Networking with district hospital for outreach cancer screening for women in the community (accessibility) • Knowing referral pathways

Discussion

Cancer Knowledge

The cancer awareness training was a pilot training for community-level healthcare providers in the Kilimanjaro Region in Tanzania. Overall, there was a significant increase in cancer knowledge in both groups.

But the increase of knowledge varied in some topics, which needs to be reflected. For example, there was a strong increase of knowledge about cancer incidence in Tanzania and about HPV, as the main cause of cervical cancer. Contrary, there was a knowledge decrease, e.g., in topics regarding risk factors, palliative care, and breaking bad news in the DHCW group. There are different factors that could have had an influence on these results: small sample size and hence small effects, some topics were only briefly discussed, some topics might have had less relevance for the participants, and/or the training methods were not eligible for all topics. Further evaluation by the trainers will be conducted to explore the reasons and the curriculum and mode of delivery will be adapted for the topics "breaking bad news," "risk factors of cancer," and "pathophysiology of cancer" as necessary.

However, the overall knowledge increased among the participants remarkably and their newly gained knowledge empowered them to apply it into their practical work in community outreach and dispensary work, as they reported in the training evaluation. Our findings confirm previous studies with similar focus on raising cancer awareness in other groups of healthcare workers in Tanzania [8, 9, 20]. Being the basis of the health system in Tanzania and often the only link to healthcare for many people, it is important to increase community-level healthcare workers' knowledge and involvement in cancer control [10]. More research is needed to analyze their role and impact on cancer control [16, 21], but we assume they play a key role in Tanzania's healthcare system.

The baseline assessment in both groups showed that a vast majority of the participants had not received previous training

Fig. 1 Pre- and post-training cancer knowledge, CHWs and DHCWs

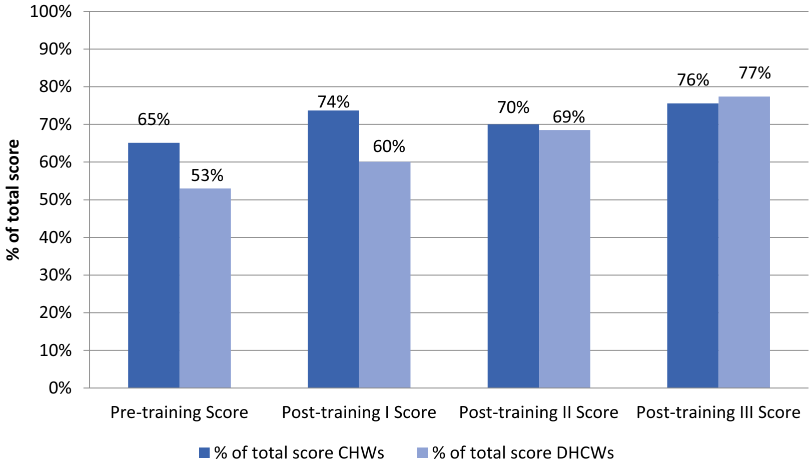
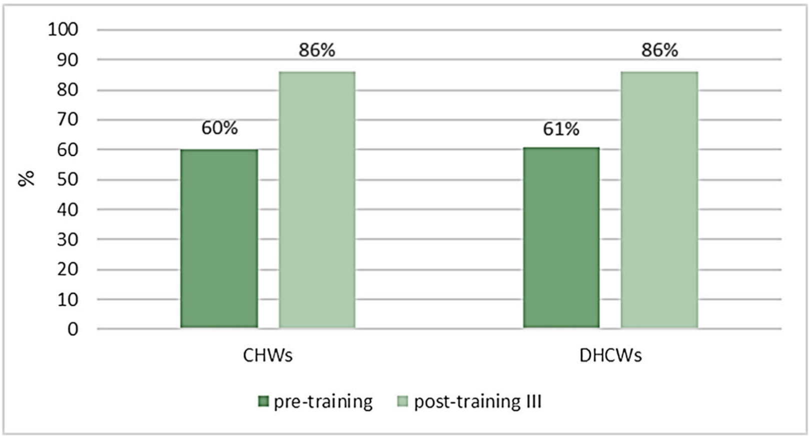


Fig. 2 Correct MC answers in %, pre-test and post-test training III, CHWs and DHCWs compared with selected questions



on cancer. Due to this gap in knowledge, CHWs and DHCWs may not be aware of early signs of cancer and lack knowledge of how to detect early stages. This is another factor stressing the importance of training to increase their cancer awareness and hence timely referral and diagnosis of the patients.

Comparing the level of cancer knowledge of both training groups before and after the training, there was no remarkable difference. Although the DHCWs were assumed to have a better prior medical knowledge, no noteworthy differences have been found in the assessment.

This surprisingly low level of knowledge of the DHCWs could have several reasons. Apart from the fact of having a small sample size in this study (and hence no generalizability can be ensued), the missing previous cancer training is very likely to be the main reason, as only one person of the group has had previous training. But also, many DHCWs in Tanzania sometimes miss comprehensive medical education. Some studies show that due to a massive shortage of the health workforce in Tanzania, DHCWs often miss comprehensive medical education [10, 17] and do not fulfill the desirable level of education (like nursing or clinical officer school). The educational background in this study group reflects that 45.5% had only completed primary school and hence do not represent the required level of education for the dispensary level.

Regardless of the pre-knowledge, this study suggests that an increased cancer knowledge in both groups lead to motivation to apply the newly gained knowledge into practice and to educate their communities. Challenges in implementing this knowledge into the community were mainly due to competition with traditional healers [22]. Consulting traditional healers is often a first health-seeking approach for many people in Tanzania, especially in rural areas, and particularly in NCDs [23].

The Role of CHW and DHCW

Another aim of PrevATrain was to educate the participants about the referral system for cancer patients in Kilimanjaro Region and to provide a clear guideline for referrals. As Kwesigabo et al. stated, poor communication between the healthcare facilities is one of the factors leading to late-stage presentation [24].

After the training, the participants were more aware about the referral pathways and the possibilities of treatment at the CCC. Participants were given a phone number, which allows them to connect directly with the respective department at the referral hospital. This possibility of having a specialist feedback encouraged the community-level healthcare providers to become more confident in their referral decisions.

The positive effects of the cancer awareness training for the CHWs and DHCWs and their involvement in cancer control underline their potential contribution to public policy objectives for comprehensive cancer control in Tanzania and many other SSA countries [21].

The MoHSW of Tanzania implemented the National Cancer Control Strategy (NCCS) [19] to address the problem of the growing cancer burden. Goal 7 of the NCCS specifically states the human resource development for cancer control on the different healthcare delivery levels [19]. Availability, accessibility, and capacity of a well-trained health workforce are necessary and cost-effective elements to deliver quality primary healthcare and are steps towards universal health coverage (UHC) [25].

Training Methods

The pilot cancer awareness training was the first training carried out by CCC. Feature of the training method is the repetitive design over three sessions. Repeating contents in learning is a common method to increase learning outcomes [26]. With a long interval between the training sessions of about 1 month, the healthcare workers had time to start applying the new cancer knowledge into their practice and exchange first experiences in the next training session. Especially, the experience sharing in small groups was very welcomed by the participants and probably contributed to the training success.

Limitations

The study aimed to test a pilot intervention in a specific chosen area, using a small purposive sample without any control group. Therefore, the findings cannot be generalized and only represent the CHWs and DHCWs who attended the training.

Conclusion

Due to the shortage of health workforce in Tanzania, educating community healthcare workers is an important part of working towards universal health coverage in Tanzania [21]. The pilot cancer awareness training by PrevATrain was successful in raising cancer awareness and confidence in cancer control of the health workers. To address the growing cancer burden, deal with the shortage of the health workforce and achieve the goal of UHC, more cancer awareness trainings for community-level healthcare providers are needed [2, 10]. The concept of repetitive cancer awareness training is a cost-effective measure and might be applicable to other low-resource settings in SSA, even though adjustments of the curriculum in some topics might be necessary.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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Alwash Z, **Henke O,** Serventi F, Kanthelhardt E. (2019) Staff Perspectives Towards Challenges in a Newly Established Cancer Centre in Tanzania: A Qualitative Study. J Glob Oncol. Mar;(5):1-8

Zielsetzung der Arbeit: Es sollte nach wissenschaftlichen Methoden untersucht werden, welche Erfahrungen und Herausforderungen unter Mitarbeiterinnen und Mitarbeitern einer neu gegründeten onkologischen Abteilung in einem LMIC-Setting bestehen. Daten zur Akzeptanz dieser für LMIC neuen Disziplin sind für SSA kaum vorhanden. Die Ergebnisse sollen wichtige Aspekte aufzeigen und bei Planungen zukünftiger Krebsbehandlungseinrichtungen helfen.

Methoden und Ergebnisse: Eine qualitative Inhaltsanalyse der Transkripte von elf Mitarbeiter/innen-Interviews wurde durchgeführt. Teilnehmer waren Ärzte/innen, Pflegekräfte, Apotheker/innen und eine administrative Mitarbeiterin. Fünf Hauptkategorien wurden identifiziert: Training und Weiterbildung, Verfügbarkeit finanzieller Mittel, Managementherausforderungen, Interesse an zukünftiger Entwicklung und Berufszufriedenheit.

Schlussfolgerungen: Fehlende oder unzureichende Ausstattung mit Personal, Ausbildung und Qualifikationen wurden als größte Herausforderungen genannt sowie der Wunsch nach finanzieller Nachhaltigkeit durch Kooperation der Regierung mit internationalen Organisationen. Die Kooperation mit einer Vielzahl an internationalen Organisationen verlangt eine Führung durch ein *Health Care Management* und kann nicht vom onkologischen Fachpersonal geleistet werden. Motivation und Zufriedenheit durch die Möglichkeit onkologische Behandlungen anzubieten, steht der geringen Gesundheitskompetenz der Patientinnen und Patienten gegenüber, die aus diesem Grund oft zu spät diagnostiziert würden.

original report

Staff Perspectives Toward Challenges in a Newly Established Cancer Center in Tanzania: A Qualitative Study

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abstract

PURPOSE Cancer is a growing public health concern in low-income countries (LICs). From 14 million new patient cases identified worldwide each year, 8 million are diagnosed in LICs. The fatality rate is 75% in LICs compared with 46% in high-income countries. Causes are low literacy levels, lack of awareness and knowledge about cancer, and limited education of health care professionals that leads to late detection and diagnosis. In Tanzania, cancer incidence will double to 60,000 in 2030. The referral hospital of Northern Tanzania established a new cancer unit in December 2016 to meet these needs. However, there is limited knowledge about perceptions of health care professionals toward cancer care in LICs. This study aims to understand attitudes and perspectives of those professionals and the treatment-related challenges in a newly established center to assist future efforts in this field.

METHODS A qualitative method approach using in-depth interviews was chosen to achieve inductive conceptualization. Analysis of data was performed according to qualitative content analysis.

RESULTS Eleven interviews were conducted. Five main categories were found: training and education of staff, availability of financial support, challenges in management, interests in future developments, and job satisfaction. Subcategories elaborated in more detail within the main categories.

CONCLUSION Limitations in staffing, training, and education were major concerns. The importance of sustainable funding and the needed cooperation of the government with international aid were identified as key points. The involvement of different stakeholders requires guidance by health care management. Health care professionals expressed their satisfaction with the possibilities of treating cancer and the rewarding feedback from patients. Misconceptions and poor knowledge by patients were mentioned as reasons for delayed health-seeking behavior. Screening and awareness programs were seen as useful interventions.

J Global Oncol.

INTRODUCTION

Although, in the past, cancer was almost exclusively an issue for developed countries, the American Cancer Society states that it is becoming more of a global health concern.[1] Cancer incidence in low-income countries (LICs) is increasing because of multiple factors, such as Westernization, changes in lifestyle, increased life expectancy, and advances in diagnostic and detection practices.[2] Half of the global cancer incidence (8 million) in 2012 was diagnosed in LICs according to the International Agency for Research on Cancer.[3] For Tanzania, cancer incidence is expected to nearly double in only 15 years, from 37,000 new patient cases in 2015 to more than 61,000 in 2030.[3]

Tanzania is one of the poorest countries in the world. A report by the Tanzanian National Bureau of Statistics in 2013 indicates that 28.2% of the population lives below the basic needs poverty line; 68% live on less than 1.25 US dollars a day, according to the World Bank.[4,5] Cancer aggravates the cycle of poverty, especially in countries with limited resources and weakened health systems.[6] Poverty is a notable barrier for seeking early medical attention.

Another important barrier to seeking early medical attention is poor literacy. Lack of awareness and knowledge about cancer is highlighted by the fact that only a minority of the population in Tanzania considers cancer a major health problem.[6,7]

Tanzania has a total population of almost 55 million[5] but has only 0.31 doctors per 10,000 people to provide medical services.[8] Until recently, Tanzania was home to only two specialized cancer hospitals: Ocean Road Cancer Institute (ORCI) in cooperation with Muhimbili National Referral Hospital in Dar Es Salaam

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and Bugando Medical Centre in Mwanza. Both hospitals face staff and equipment shortage,[9] which makes it more challenging to provide quality health services to a large number of patients.

Regarding training and education, two postgraduate Masters programs at Muhimbili National Referral Hospital are available: Master of Medicine in Clinical Oncology and Master of Medicine in Hematology and Blood Transfusions. Postgraduate hematology-oncology education for nurses is not available in Tanzania, but efforts have been made to introduce short educational courses.[10]

In the past decade, the Tanzanian government has recognized the need for cancer treatment and accordingly started funding ORCI to support early detection programs and to provide services to patients who need chemotherapy and radiation treatment. However, the number of patients is exceeding the capacity of the hospital.[7]

With the initiative to address the needs of patients with cancer, Kilimanjaro Christian Medical Centre (KCMC), the tertiary hospital of the Northern Zone of Tanzania, established a new cancer care center (CCC) in December 2016.

Establishment of the CCC is planned in three phases. The first phase, which started in December 2016, provided an outpatient clinic and chemotherapy infusion unit. Although many patients are also treated as inpatients in their respective departments, these inpatients are seen by the specialists on a consultation basis. The second phase, which is starting in 2019, will be the construction of an oncology inpatient ward and a patient hostel, which will be instrumental for patients who do not need inpatient care but need to travel long distances for treatment. The final, third phase, which is planned for 2021, will be a radiation unit.

During the first year of operation, two specialized physicians, four nurses with oncologic training, one specialized palliative care nurse, two pharmacists, one administrative staff, and one public health officer were employed at the CCC. Approximately 900 patients attended the service at CCC in more than 3,000 appointments, and 400 patients received chemotherapy in 2017.

Funding of the CCC is a joint effort lead by the US-based Foundation for Cancer Care in Tanzania, the Tanzanian Government, and the Evangelical Lutheran Church of Tanzania with their partnering organizations in Germany.

Cancer treatment with all its implications has not been widely studied in Sub-Saharan Africa. Cancer treatment is a new medical service provided by the CCC, so this study aims to document and analyze the attitudes and perspectives of health care staff toward chemotherapy and the challenges they face on a daily basis at their workplace. This understanding will help explore the service-related spectrum of challenges that occur in LIC settings.

METHODS

Methodologic Approach and Study Design

The research field is widely unknown, so we chose the grounded theory approach to “elicit each participant's interpretation of his or her experience.”[11] This approach assures an understanding of the participants’ viewpoints and their own concepts of work in cancer care. By using in-depth interviews as a qualitative and comprehensive approach, an inductive conceptualization of the topic can be achieved.

Sampling and Participants

All professional staff members working for the new CCC when the study was conducted were interviewed. The characteristics of the participants are listed in Table 1.

Data Collection and Analysis

After extensive narratives of the participants were obtained through open-ended questions, semistructured interviews followed to focus on specific topics: the experience of each participant about handling chemotherapy and working at the CCC, the challenges he or she faced on a daily basis, and possible suggestions for improvement.[12] The interview guideline was based on literature review and discussions made with key persons in and outside KCMC before data collection. The professional background of the interviewees was taken into consideration during the guideline design and during the interviews.

Analysis of data was performed according to qualitative content analysis and followed the steps of inductive theme formation, context analysis, and structuring.[13] Analysis was conducted by two researchers independently to assure validity.

The study was approved by the board of the Ethic Committee of Kilimanjaro Christian Medical College. The study also followed guidelines of Good Research Practices according to the Declaration of Helsinki of the World Medical Association.

TABLE 1. Characteristic of Interviewees

Profession	Age (years)	Years of Professional Experience	Sex
Physician	20-29	1	Female
	30-39	7	Male
	30-39	7	Male
	30-39	5	Female
Pharmacist	30-39	4	Male
	30-39	10	Female
Nurses	40-49	10	Female
	30-39	5	Female
	40-49	7	Female
	40-49	12	Female
Management	40-49	10	Female

RESULTS

In total, 11 interviews were conducted between March and May 2017. Interviews were conducted by the first author and lasted between 20 and 60 minutes.

As a result of the interview analysis, five main themes were identified: training and education of staff, availability of financial support, challenges in management, interests in future development, and job satisfaction; corresponding subthemes were explored (Table 2). Corresponding quotations are displayed in Table 3.

Training and Education of Staff

This main theme contains all assertions about professional training of the interviewees themselves or of the CCC staff in general. In addition, the theme contains related issues connected to professional education.

Fear of handling chemotherapy. One of the most prominent findings, mentioned by every participant, was fear of handling chemotherapy. Health care staff expressed distress about handling chemotherapy: they feel concerned about a high risk of suffering toxic effects of the medication in the future as a result of exposure, especially when they prepare the chemotherapy without using proper protective equipment. This issue was not asked about by the interviewer in particular; however, it was mentioned in response to the open-ended question.

Guidance for safe handling. Because this was a new field for the staff, they mentioned a critical need for guidance about how to handle chemotherapy safely and properly and how to store it.

Need of trained personnel. The interviewees shared a common view that the CCC was understaffed, especially with the increasing number of patients. In addition, the staff expressed their need for more training.

TABLE 2. Themes and Subthemes

Theme	Subtheme
Training and education	Fear of handling chemotherapy
	Guidance for safe handling
	Need of trained personnel
Availability of financial support	Lack of proper facilities
	Shortage of medications and equipment
	Sustainability concerns
Challenges in management	Responsibilities of staff
	Organizational strains
	Overwhelming number of patients
Interests in future development	Responsibility of politics and governmental support
	Dependency on international funding
	Learn from experienced hospitals
Job satisfaction	Effective treatment
	Making progress

Conversely, some nurses mentioned their worries about not giving patients optimal counseling because of limited time capacities. They also expressed that adequate training and increased staff members would lead to a better outcome.

Some of the nurses expressed their difficulties in venipuncture, especially when under time pressure. Sometimes venipuncture required more time for each patient, so it added more stress about the understaffing issue.

Availability of Financial Support

Financial difficulties and limited resources were mentioned by the CCC staff in different ways. They expressed the need for more financial support to improve health care facilities, to increase the availability of medications and equipment, and to provide assistance to patients with cancer.

Lack of proper facilities. CCC staff noted their need for improved facilities that would offer better infrastructure, such as a laboratory for the cancer center with standardized testing procedures and more equipped chemotherapy rooms.

Shortage of medications and equipment. Some of the health care staff stated their concerns about the availability of medications and of necessary equipment for safe-handling procedures. Although donations can be helpful for the newly established CCC, especially because it operates in an LIC setting, some donations were not fit for the purpose and not suitable for the setting.

Sustainability concerns. Apprehensions were expressed about the sustainability of the CCC service, because it is based mainly on international funding.

Challenges in Management

The staff faced various operational issues that were hindering efficiency in the work place. In particular, the dynamics of a newly established cancer treatment facility, with many different stakeholders involved, would lead to unforeseeable hurdles. The following subthemes were identified:

Responsibilities of staff. Staff noted that division of labor and definition of tasks were not clearly enough defined between different specialties, which caused duplicate or unattended responsibilities.

Organizational strains. The other management issue mentioned was lack of organizational arrangements on a day-to-day basis at the CCC, and its effects were noticed in many aspects, such as delays in the patient test results. A physician mentioned that CCC was still going through phases of out-of-stock equipment because of the lack of organizational skills to audit the stock and order equipment timely. Use of more standardized measures was mentioned as a way to enhance efficiency for the daily work routine.

Overwhelming number of patients. Unprecedented, overwhelming numbers of patients for diagnosis and treatment created more challenges in the management of the center, as mentioned by many interviewers.

TABLE 3. Themes and Subthemes With Quotes

Theme/Subtheme	Quotation
Training and education of staff	
Fear of handling chemotherapy	"Most of the time you are giving it [chemotherapy] you are not at peace at it what if something goes wrong what if I start getting the effect?"
	"I am worried of the leakage of chemotherapy, my worry is suffering later in the future, so we need more and more protective gear."
Guidance for safe handling	"Knowledge is needed in terms of handling in terms of preparing in terms of storing."
	"There has been some incidence yeah like you know they may not be able to actually intervene like they may not know how to tackle the issue and how to handle spillage or infiltrations [of chemotherapy] and so that may worry me."
Need of trained personnel	"By then we did not have trained personnel to give chemotherapy, who has the knowledge in terms of prescribing and giving."
	"So, it's basically supervisions and the need to train people, that's the bottom line so whether we can have short term plans like short courses on safety and how to handle, then we have to employ people who really have skills, especially pharmacist that, have skills and training to prepare and provide."
	"Because our patients are the long-term ones; they're angry, they need more time to talk with you. If you have many patients you can't talk with them; you hurry-hurry and you leave the patient not understanding what is going on. But if we have more staff, enough staff, then we can improve our center."
	"Sometimes we have like 12 patients there for chemotherapy for two nurses and for me it is a challenge to get the vein, it's an issue. It might take more than 30 minutes for one patient looking for a vein. So sometimes we take a long time, so we need a staff who can get, at the cancer center here because for infusion time."
Availability of financial support	
Lack of proper facilities	"We don't have our own laboratories so we are demanding or we're depending on the hospital or the outside so even to control the results."
	"Now we are serving 15 patients so even if we can have more staff the chairs we have cannot accommodate more than 20 patients so we need even more chemotherapy chairs."
Shortage of medications and equipment	"Some of the medicine are out of stock, so that's a big challenge, some patients come already on the chair and then this medicine is not available."
	"This is a new center, sometimes we need some materials, for example sometimes we need the mask, the bottles; there are special bottles for that chemotherapy. Our bottles are plastic ones. When we put your IV given and they spill up the chemotherapy into the floor so that is not good so we need some equipment."
	"I feel well protected but sometimes you're missing some of the PPE, sometimes maybe the mask is over, there is no replacement; the goggle is over, there is no replacement. But when we have those I feel like protected."
	"In the clinic such as image viewing like x-ray image viewing like obviously it was donated but we don't have the appropriate voltage and so on and so we have to buy stabilizers and you know things to actually make it work."
Sustainability concerns	"Challenge is sustainable availability of chemotherapy because they're expensive and we don't have a sustainable way of maintaining that so you know some drugs run out and we have no access to them."
Challenges in management	
Responsibilities of staff	"I think it's not very, very, very clear in terms of line of responsibilities that are supposed to be done by clinicians, what is supposed to be done by oncologists, what needs to be discussed you know stuff like that."
Organizational strains	"Some patients we had to postpone the chemotherapy because we couldn't see some of the results."
	"We haven't created a system where we actually buy those equipment before they run out."
	"Second is the arrangement maybe, it's not set yet, so we see that the file comes even the medicine is written paclitaxel [chemotherapy drug] this and this, they are not directly instructions as the protocol says."
	"I think it's clear information, a clear set-up plan for all the files and the clinics we should have a schedule maybe, people should follow the schedule, they should know that these patients have to be seen by the doctor, protocol have to be clear before anything goes to the pharmacy."

(Continued on following page)

TABLE 3. Themes and Subthemes With Quotes (Continued)

Theme/Subtheme	Quotation
Overwhelming number of patients	"What worries me, is now the number of patients now we're actually having more and more. Now a worry would be if it's quite a lot of patients and we don't have enough of the chemotherapy agents."
	"From the beginning, I think we didn't expect to have much patients but now the Minister has announced people are coming from Northern zone, then don't to go for the Ocean Road for the chemotherapy, they have to be referred to the KCMC so we're expecting four hundred patients per year but now we are, not even the mid of the year, we have five hundred patients."
Interests in future development	
Responsibility of politics and governmental support	"I guess we still have to do, the policy makers, the health policy makers, I know they are right now fighting so hard, they are trying to make that the treatment be free for all children under 5 with malignancies, but we are not yet there."
	"We need to act fast and try and get the government involved and support as much as I can to make the medications even available within our country."
	"When we're trying to ask the patient to contribute to that they say that cancer patients have to get free treatment that's the word that they hear from the government while we don't have any money from the government or any drugs from the government. Now all chemotherapy from the government has been allocated into the Ocean Road but maybe this year we may get some."
Dependency on international funding	"The chemotherapy which we are receiving now is from donors, so someone is giving us, donating these drugs for free and the worries that one day that might run out and you know that they are very expensive and an average Tanzanian citizen cannot afford and the majority of our citizens are not insured."
Learn from experienced hospital	"Right now, we are trying to see what other people are doing and we try and incorporate it to us."
	"Go visit places that have proper chemotherapy, so in Tanzania its Ocean Road where they are providing, and there is Buganda hospital which is another hospital providing, spend time with the other staff who are providing. Bottom line is supervisions and the need to train people."
Job satisfaction	
Effective treatment	"There is a big level of excitement because we're treating now and we're using chemotherapy and like you know we're administering it and knowing side effects and knowing how to handle it and educating patients on the side effects, letting them know what to expect from the chemotherapy so I think that is a big achievement."
	"I think it's a good opportunity to do it, for us to treat these people and with the aid, with the sponsorship which we are getting, I think it's wonderful and we would lots of patients here comes and gets medicine and pediatrics are getting chemotherapy."
	"My biggest achievement and my biggest fulfilment is seeing patients getting cured especially patients who were not able to afford chemotherapy."
Making progress	"Actually, I am relieved, right now and quite happy because right now I see that chemotherapy is given in the proper way and being stored in the propped way and we have proper protective gear right now, so the risks are minimal right now."
	"What keeps me positive you know what I see positive is that everyone is trying as best possible to do their part yeah, there are weaknesses and there are you know we're still working on them but I think it's good you know I think it's good yeah for what we have achieved so far."

Abbreviations: IV, intravenous; KCMC, Kilimanjaro Christian Medical Centre; PPE, personal protective equipment.

Interests in Future Development

The health care providers expressed their huge interest in the development of the CCC, and they identified some of the intertwined factors that played a paramount role in the development process:

Responsibility of politics and governmental support. The care providers mentioned the importance of the local government's role in providing future support to the CCC. This support could be manifested in policy making, such as financial support to the Tanzanian citizens diagnosed with cancer.

Another way in which the government could play a role is by assisting in the provision of medications and by making medicine available on a local level. One of the participants mentioned that the financial support was directed to the government-run ORCI. However, as per the government plan, the target was to decentralize cancer services to other regions in the country. This process, however, has not yet reached KCMC, and the delay was creating financial strains.

Dependency on international funding. The health care staff expressed their current worry about their dependency on international donors to provide the needed medications and equipment. This dependency raises concerns about sustainability and continuity of the provision of services in the future.

Lessons from experienced hospital. Some of the health care providers proposed learning from other hospitals that have experience in this field and a similar low-resource setting, like ORCI or the Bugando Medical Centre. This suggestion could be helpful because of the common context that these centers share.

Job Satisfaction

Besides the challenges and obstacles in the delivery of chemotherapy, the interviewees expressed their satisfaction about working at the CCC.

Effective treatment. The possibility of having an effective treatment of cancer, which was lacking, was an exciting experience for the health care professionals (HCPs). The joy of getting a rewarding feedback by curing patients or at least by reducing their burden of symptoms also was mentioned, especially by the nurses.

Making progress. Regardless of the problems mentioned, the staff of the new established CCC appreciated the progress in their field of work.

Differences Among Groups of Interviewees

Generally, the answers of the HCPs were consistent throughout all professional groups. With regard to the fear of handling chemotherapy, responses depended on previous experience and level of exposure to chemotherapy. Those HCPs involved in handling, reconstitution, or administration of chemotherapy expressed more concerns. Female professionals were especially concerned about the influence of handling chemotherapy on their reproductive health.

DISCUSSION

This study explored the attitudes and perspectives of health care staff toward cancer care in a newly established treatment facility in a low-resource setting.

One theme mentioned by all participants was the strong need for more oncology training. This finding resembles results of previous research. In a Knowledge, Attitudes, and Practices study conducted with medical staff in Uganda, less than 40% were aware of the risk factors for cervical cancer.[14] Rick et al[15] displayed that the baseline knowledge among HCPs about cancer was limited in an urban Tanzanian setting. Additional studies have shown that poor baseline understanding of cancer and chemotherapy exists among medical staff in Tanzania and concluded that there was a need for continuous medical education and training.[15-17] The same findings were highlighted by Makani et al[18] about knowledge in hematology among Tanzanian HCPs.

In this study, many participants mentioned that sufficient oncology training was lacking before they started working at CCC. Thereby, the nurses in particular played an important role to provide care and deliver services to patients through monitoring of physical conditions and administration of chemotherapy. In addition, they helped counsel patients and families about medical conditions and the expected adverse effects of the treatment.

Despite partial funding by international donors, the insufficient level of financial support at CCC was another main concern. That manifests itself in two dimensions: the lack of proper facilities and shortages of medication and equipment, and the concern about future sustainability of these international funds and so the continuity of the CCC itself.

The financial concern is closely interlinked with the abovementioned fear of handling chemotherapy: When inadequately trained staff and a lack of standard operating procedures are coupled with equipment shortages (in particular, protective gear), HCPs lack confidence to perform daily tasks, and their fear is reinforced.[19]

However, the interviewees expressed satisfaction with the achievements so far, especially that effective treatment options were available for patients with cancer. Furthermore, rewarding feedback from the patients was another positive aspect for the HCP. These findings are consistent with a study from Kamisli et al[20] among Turkish oncology nurses, in which nurses indeed expressed their exhaustion but also their increased levels of empathy, patience, awareness about priorities in life and job satisfaction. Despite an excessive workload, Australian oncology nurses showed high levels of personal satisfaction and personal accomplishments in a survey among 234 nurses.[21] That job satisfaction among this group can be enhanced by a good physician-nurse relation, the freedom to make patient-care decisions, and appropriate staffing was stated in a Canadian survey.[22]

Health care management was another concern for the HCPs. This concern manifested as difficulties in efficient provision of services, such as having test results prepared before the next chemotherapy cycle, having an electronic inventory system for medications to have necessary stock always available, and not having standardized treatment protocols.

Management and leadership are vital for good health governance. As a health governance report by the United States Agency for International Development stated, it is important to have governance in addition to operational capacity when delivering health services.[23] Organizational strains, lack of recognition and support from management, and unrealistic expectations were also associated with lower job satisfaction and higher burn-out rates among New Zealand oncology HCPs.[24]

Limited management capacity was negatively affected by the unprecedented number of patients visiting the center. When the study was conducted, only four nurses and one full-time pharmacist were assigned to CCC to provide services for approximately 180 chemotherapies monthly. As of 2018, after the increased public awareness of cancer that resulted from media coverage of the services provided, CCC expected to receive approximately 600 additional patients annually, according to the executive director of KCMC.[25,26] This increase could create more strains on the availability of medications and equipment and also may affect the quality of services.

The study results were used to shape the functionality of the center. Standard operating procedures for chemotherapies have been implemented, and managerial issues were resolved by implementing the position of a clinic administrator who oversaw funding, procurement, and patient flow. A training about safe handling of chemotherapy conducted by the German Institute for Medical Mission was extended to respond to the fear of handling. Continuing medical education for the staff was implemented as internal and external trainings in regular intervals. Currently, staff numbers have increased and the government has contributed to medication on a large scale.

Although all interviewees received their professional education in the English language, a limitation could be loss of information by not presenting information in Swahili. The study was conducted shortly after the opening phase of the CCC. Therefore, the results must be interpreted with this background. Nonetheless, this timing is also a strength, because it provided insight about the problems during the implementation phase and could serve as a guidance for similar centers.

As cancer burden increases continuously, increasing numbers of patients in the few available cancer treatment facilities in Tanzania are expected. Adequate numbers of qualified HCPs must be trained and available from the early stages of new facilities. Provision of standard operating procedures for cancer treatment could help streamline daily work tasks. The NCCN guidelines for Sub-Saharan Africa[27]—as well as the national guidelines of Tanzania, which are expected to be released in 2019—could be instrumental. Because cancer care in an LIC is costly, coordination with health insurances, donors, non-governmental organizations, pharmaceutical companies, and other stakeholders is an important management task that must be addressed by health care management professionals.

Collaboration with existing cancer treatment facilities in an LIC can provide expertise and synergy for new centers. To create resilience among oncology nurses, an interventional study from Poulsen et al[28] showed that a 1-day interventional workshop has the potential to enhance resilience, prevent burn-out, and increase satisfaction with current self-care.

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Leak SA, Mmbaga LG, Mkwizu EW, Mapendo PJ, **Henke O**. (2020) Hematological Malignancies in East Africa – Which cancers to expect and how to provide services. PLoS ONE 15(5): e0232848

Zielsetzung der Arbeit: Die malignen hämatologischen Erkrankungen, die im Cancer Care Centre des KCMC behandelt wurden, sollten analysiert werden, um Charakteristika und klinische Präsentation tansanischer Patientinnen und Patienten besser zu verstehen. Zudem sollte der Aufbau des hämatologischen Behandlungsangebots als Modellprojekt für zukünftige Behandlungszentren in ähnlichen Settings deskriptiv dargestellt werden.

Methoden und Ergebnisse: Retrospektive Querschnittsanalyse der Krankenakten aller Patientinnen und Patienten mit hämatologischen Neoplasien des Zeitraums Dezember 2016 bis Mai 2019 sowie narrative Deskription des Aufbaus von Diagnostik und Therapie im LMIC-Setting. 209 Patientenakten konnten ausgewertet werden. Die häufigsten Diagnosen waren NHL und MM. Die häufigste NHL-Entität stellte die CLL/SLL dar. Mehr als die Hälfte der CML-Patientinnen und Patienten waren jünger als 40 Jahre. Die Geschlechter waren insgesamt gleich häufig vertreten, während unter den CLL- und HL-Patientinnen und Patienten Männer häufiger vertreten waren. Ein zweiter Altersgipfel bei älteren Patienten mit HL wurde nicht beobachtet.
Zum Aufbau hämatologischer Diagnostikkapazitäten wurde zunächst die existierende Laborinfrastruktur des KCMC genutzt und später durch ein eigenes Hämatologielabor im CCC ergänzt. Dabei spielten internationale Kooperationen mit NGOs und *„Free Access to Medicine Programmes“* eine ebenso tragende Rolle wie Forschungskooperationen.

Schlussfolgerungen: Hämatologische Erkrankungen traten in einem jüngeren Alter und höheren Stadien auf im Vergleich zu publizierten Daten aus dem globalen Norden. Erklärungsansätze können neben der Demographie Tansanias die hohe Infektionslast in den (Sub-) Tropen und Umweltfaktoren liefern. Das konsequente Nutzen von lokalen Synergien und internationalen Partnerschaften ist dazu geeignet einen hohen Qualitätsstandard in der Diagnostik aufzubauen und zu erhalten.

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RESEARCH ARTICLE

Hematological malignancies in East Africa—Which cancers to expect and how to provide services

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Abstract

Background

Sub-Saharan Africa (SSA) has an increasing non-communicable disease burden. Tanzania has an incidence of more than 35,000 cancer cases per year with an 80% mortality rate. Hematological malignancies account for 10% of these cases. The numbers will double within the next 10 years due to demographic changes, better diagnostic capabilities and life style changes. Kilimanjaro Christian Medical Centre established a Cancer Care Centre (CCC) in December 2016 for a catchment area of 15 million people in Northern Tanzania. This article aims to display the hematological diagnosis and characteristics of the patients as well as to describe the advancements of hematologic services in a low resource setting.

Methods

A cross-sectional analysis of all hematological malignancies at CCC from December 2016 to May 2019 was performed and a narrative report provides information about diagnostic means, treatment and the use of synergies.

Results

A total of 209 cases have been documented, the most common malignancies were NHL and MM with 44% and 20%. 36% of NHL cases, 16% of MM cases and 63% of CML cases were seen in patients under the age of 45. When subcategorized, CLL/SLL cases had a median age was 56.5, 51 years for those with other entities of NHL. Sexes were almost equally balanced in all NHL groups while clear male predominance was found in HL and CML.

Discussion

Malignancies occur at a younger age and higher stages than in Western countries. It can be assumed that infections play a key role herein. Closing the gap of hematologic services in SSA can be achieved by adapting and reshaping existing infrastructure and partnering with international organizations.

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Introduction

We live in an increasingly interconnected, global community with a fast-growing population. On one hand, we see rapid advances in healthcare as a result of global cooperation, while on the other hand, disparities in health care are becoming more apparent. Sub Saharan Africa has an exponentially increasing healthcare need; currently estimated to have 25% of the global disease burden. In addition to health stressors including HIV/AIDS and resurgent epidemics; Africa also faces an ageing population, and an increasing non-communicable disease burden [1,2].

In 2008 the incidence of cancer cases in Africa was estimated to be 681,000 with a mortality of 512,000 [3]. Without considering changes in incidence rates, projections suggest that these figures are likely to rise to 1,27 million and 970,000 respectively by 2030 [3]. In Tanzania alone, more than 35,000 new cancer cases per year are reported, with a mortality rate reaching nearly 80% [4]. Hematological malignancies including Hodgkin lymphoma (HL), Non-Hodgkin lymphoma (NHL), leukemia and Multiple Myeloma (MM) currently account for approximately 10% of these cases [5].

Kilimanjaro Christian Medical Centre (KCMC) based in Northern Tanzania with predominantly rural areas and two main urban centers, Moshi and Arusha. Until 2016, the majority of diagnosed malignancies were referred to the governmental Ocean Road Cancer Institute (ORCI), located in the 550 km distant city of Dar Es Salaam, for their ongoing management and care. As a result, loss to follow up and presentations at late stage were significant problems. Recognizing the needs, KCMC established its own Cancer Care Centre (CCC) in December 2016 to provide accessible service to the catchment population. The centre consists of two buildings containing a small laboratory, two consultation rooms, a procedure room, 16 outpatient chemotherapy bays, waiting area and two administrative offices.

KCMC harbors one of three cancer registries in Tanzania, the other two being based at ORCI, and Bugando Medical Centre in Mwanza. These databases used to rely mostly on diagnosis made by the respective Pathology Departments, hence hematological malignancies diagnosed by other means including polymerase chain reaction (PCR), karyotyping, flow cytometry and/or blood smear cytology are not well documented. As a result of these shortcomings and other factors, reliability of epidemiological cancer data, and of hematological cancer data in particular, can be considered as weak [6].

This paper should serve two purposes: First, to describe the various hematological malignancy cases which have presented to CCC and the associated clinical and demographic factors. Secondly, to highlight the challenges in managing these cases in a resource limited setting as well as providing solutions by displaying our approaches for the improvement of diagnostics, treatment and overall patient care.

Methods

Study setting

CCC is based in the city of Moshi within the Kilimanjaro region in Northern Tanzania. The catchment area of this Department consists of the regions Kilimanjaro, Tanga, Manyara, and Arusha with a total population of approximately 15 million. Despite the two urban centres Arusha City and Moshi, the area can be described as rural. CCC is accessible through the main road of the country, connecting the cities in Northern Tanzania with the economical center of Tanzania Dar Es Salaam in the East, Arusha and Mwanza in the West and the capital of Tanzania, Dodoma, in the South. The transport infrastructure outside the main routes are mainly gravel roads and impose difficulties to travel, especially during the rainy season.

Study period and design

We conducted a cross-sectional analysis of all hematological malignancies from the cancer registry of CCC from its establishment in December 2016 until May 2019.

A convenient sampling of all recorded cases of hematological malignancies in CCC´s cancer registry has been applied. The collected data were: Diagnosis, age at time of diagnosis, sex and stage of the disease (where available). Diagnosis were categorized in to 6 main groups: HL, MM, NHL, chronic myeloid leukemia (CML), acute myeloid leukemia (AML), and acute lymphoblastic leukemia (ALL) including staging, sex and age at diagnosis. NHL cases were further subcategorized into the most common entities, diffuse large cell lymphoma (DLCL), Chronic lymphocytic leukemia/Small lymphocytic lymphoma (CLL/SLL) and other NHL cases. Median age at diagnosis and interquartile range (IQR) were calculated for each group, the sex ratio and clinical staging were also displayed.

A descriptive report provides information about the development of diagnostic means, and treatment advances through cooperation and using synergies of existing structures.

Ethical considerations

Ethical clearance was granted by the Kilimanjaro Christian Medical College Research Ethics and Review Committee in accordance with the Declaration of Helsinki. Informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data.

Results

During the report period, 209 cases of hematological malignancies were documented in the cancer registry of the CCC. Table 1 shows the cases by age and sex distribution. Table 2 shows the sub-categorization of NHL cases. The most common malignancies seen were NHL and MM accounting for 44% and 20% of cases respectively. 36% of NHL cases, 16% of MM cases and 63% of CML cases were seen in patients under the age of 45. When cases of NHL cases were subcategorized the median age was 56.5 for those with CLL/SLL and 51 years for those with other entities of NHL. Sexes were almost equally balanced in all NHL groups while clear male predominance was found in HL and CML.

The majority of cases were in stage 3 or 4 (according to Ann-Arbor classification) and in stage 3 according to Binet and Salmon and Durie classification at the time of diagnosis (Fig 1). Fig 2 demonstrates that age distribution of Hodgkin lymphoma and CLL/SLL cases.

Table 1. Hematological malignancies, subcategorized by entities and age groups.

Age	Hodgkin Lymphoma	Non-Hodgkin Lymphoma	Multiple Myeloma	AML	ALL	CML
Total (209)	18	92	43	15	17	24
0–14	2	3	0	2	7	2
15–24	7	9	3	2	9	0
25–44	6	21	4	7	0	13
45–64	3	36	25	4	1	9
65+	0	23	11	0	0	0
Median age at diagnosis	23.5	54	58	35	15	42
IQR	10 (18.3–28.3)	25.5 (38–63.5)	13.5 (51.5–65)	21.5 (21–42.5)	13 (4–17)	17.5 (35.5–53
male:female ration	2.6:1	1.1:1	1.3:1	1.1:1	1.8:1	2.4:1

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Table 2. CLL/SLL, DL(B)CL and other NHL categorized by age groups.

Age	CLL/SLL	DL(B)CL	Other Non-Hodgkin Lymphoma
Total (92)	40	10	42
0–14	0	0	3
15–24	4	1	4
25–44	8	3	10
45–64	16	4	16
65+	12	2	9
Median age at diagnosis	56.5	54.5	51
IQR	28.5 (40–68.5)	19.8 (39.8–59.5)	30.8 (31.8–62.5)
male:female ratio	1:1	1.5:1	1.1:1

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Establishing the Cancer Care Centre

Initiated by the Foundation for Cancer Care in Tanzania (FCCT), a US based non-governmental organization, funds were allocated to KCMC for the construction of two buildings; an outpatient clinic and an infusion centre, that represent the KCMC Oncology Department (CCC). Due to sparse specialized staff resources in the field of Hematology and Oncology, a KCMC nurse was sent to Duke University Oncology Department (North Carolina, USA), for

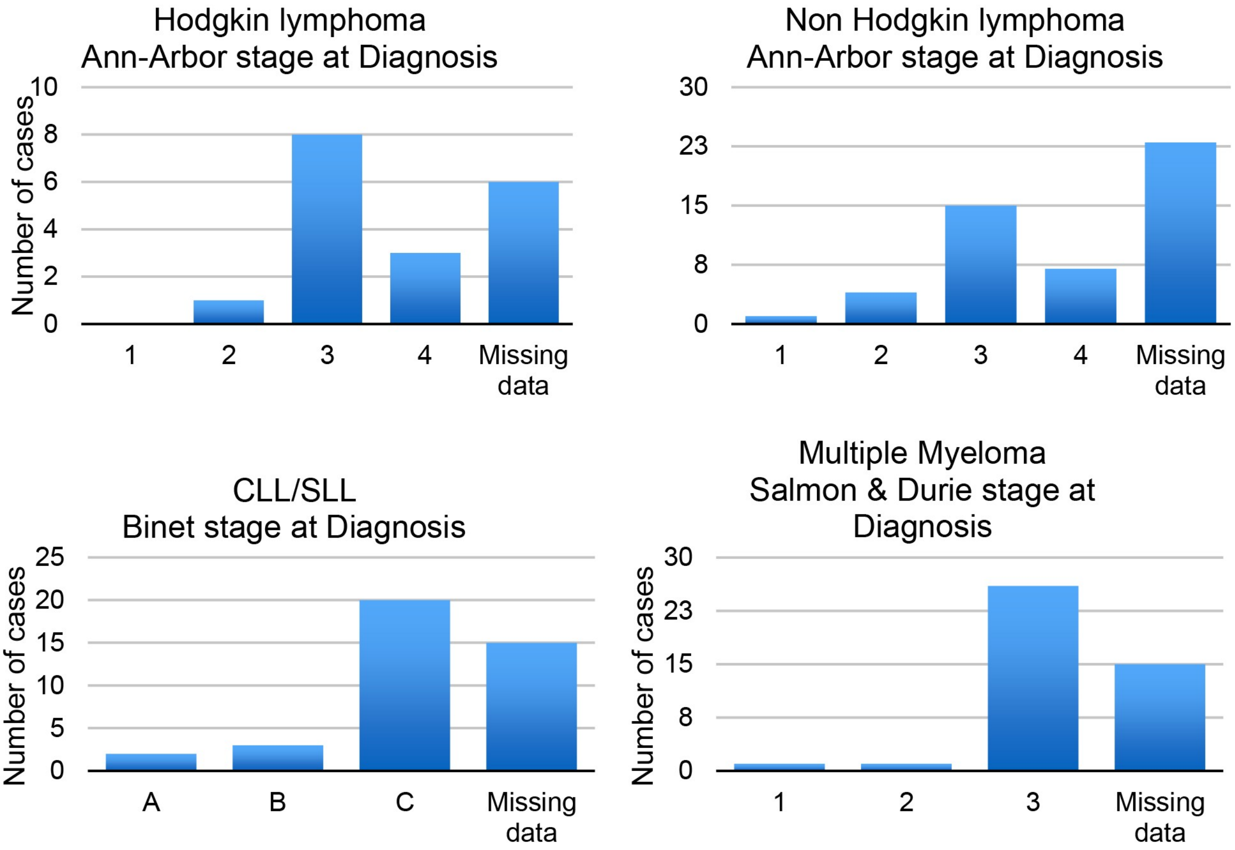

Fig 1. Ann-Arbor staging for Hodgkin and Non-Hodgkin lymphoma cases, Binet stage for CLL/SLL cases and Salmon & Durie stage for MM cases at diagnosis.

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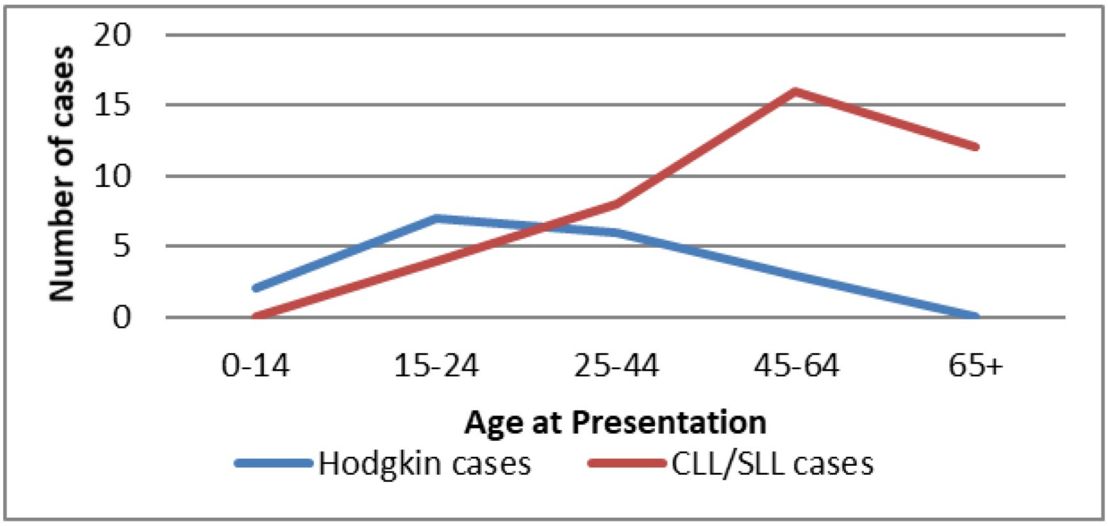

Fig 2. Cases of Hodgkin lymphoma and CLL/SLL per age category December 2016—May 2019.

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specialized training in administering chemotherapy in early 2016. A Tanzanian Oncologist and Radiation Specialist, trained in South Africa, was recruited through FCCT to lead the Centre. Another specialized doctor (Hematology and Medical Oncology) and a Public Health officer were recruited as development aid workers from a German Lutheran Mission (Mission Eine Welt) and a Tanzanian Clinic Coordinator was employed. These workers represented the workforce before the Centre was officially opened, to plan the integration of the new Department into the structure of the hospital, write up therapy protocols and standard operation procedures, explore procurement pathways and public relation, and to discuss prevention campaigns strategies. Supported by various short-term volunteers from abroad, that focused on hands-on training for additional KCMC staff that was subsequently allocated to the new Centre.

At the time of opening, 3 additional nurses and a pharmacist were permanently allocated. Fig 3 displays the further staff development in the following years with the addition of assistant doctors (registrars), a second specialist in Hematology, social worker and additional administrative staff.

As part of the tertiary hospital KCMC, radiology and pathology diagnostics and a main hospital laboratory were available from the beginning, even though special hematological investigations were not being offered and Giemsa stained peripheral blood or bone marrow aspirations smears were the only diagnostic means in the beginning. After recruiting a laboratory scientist, a small CCC hematology laboratory was opened, starting with a microscope and manual Giemsa, Sudan Black and Myeloperoxidase staining only. The necessity of blood tests prior to every cycle of chemotherapy, the investment in blood count and biochemistry machines was reasonable and empowered the small laboratory to work economically and sustainably through reimbursements of standard biochemistry and blood count tests.

A Flow Fluorescence-activated Cell Sorting (FACS) machine ("FACScalibur", BD Medical) was installed in the main hospital laboratory for CD4 counts of HIV patients. These machines are widely distributed in Sub Saharan Africa by the PEPFAR (The United States President´s Emergency Plan for AIDS relief) program for CD4 counts. Due to the favorable use of viral load instead of CD4 counts in more recent times, the machine was mostly not utilized, which gave CCC the chance to procure reagents and reactivate the FACS for leukemia and lymphoma diagnostics, without investing in a new machine.

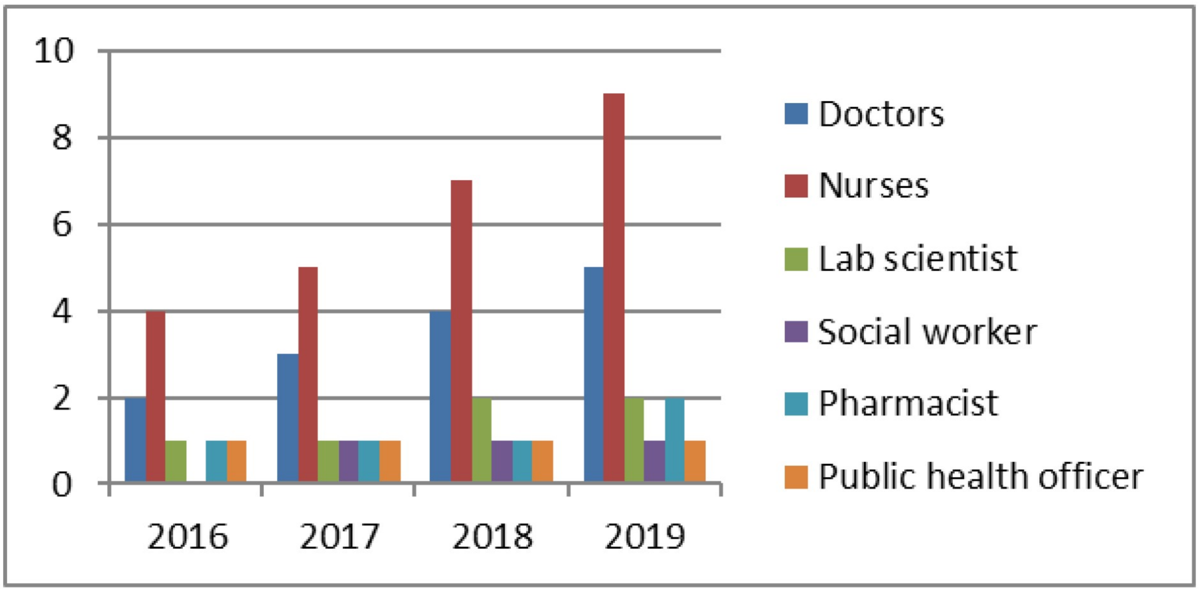

Fig 3. Development of permanent staff at the CCC since its establishment.

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The same approach was used with the polymerase-chain-reactions (PCR). The widely available GeneXpert (Cepheid) machines in Sub-Saharan Africa for tuberculosis testing, can now be adapted for BCR-ABL fusion gene diagnostics. Just as with the FACS machine, procurement of cartridges remained the only costs for the Centre.

Collaboration and partnering with various international organizations, was—and still is—a mainstay of the CCC´s functionality. The MAX Foundation (former Gleevec International Patient Assistance Program) partnered with CCC in August 2018 and continues to deliver first and second-line therapies for CML patients on a no cost basis and supports procurement of discounted PCR cartridges as well. The German Institute for Medical Mission (DIFÄM), a long-standing partner of KCMC, expanded its support to the CCC with the procurement of standard chemotherapies and facilitates the Centre with protective garments for safe mixing and administering of cytotoxic medications. In addition, annual hands-on trainings on site, is conducted by an experienced pharmacist from DIFÄM. FCCT and the German-Bavarian Lutheran Church are strong partners for donations of equipment and funding of various programs of the CCC (palliative care delivery, prevention and awareness programs). Through the American Society of Clinical Pathology (ASCP), the Pathology Department of KCMC was equipped with a telepathology machine and immunohistochemistry reagents.

The Centre has received several volunteers throughout the years. Especially senior experts with decades of experience in their respective fields are of great value for the few specialists in the Centre to discuss treatment protocols and approaches adapted to the Tanzanian setting. On the other hand, the Centre sends staff abroad, for exposure to high resource settings where ideas can be gained and implemented in an adapted way for the CCC setting.

Figs 3 and 4 demonstrate how staff recruitment, diagnostic means and treatment options have evolved at CCC since its establishment in 2016.

Discussion

Prior to 2016, hematological malignancies were underrepresented in the Kilimanjaro Cancer registry. Lack of formal diagnosis in the absence of available services, and limitations in case

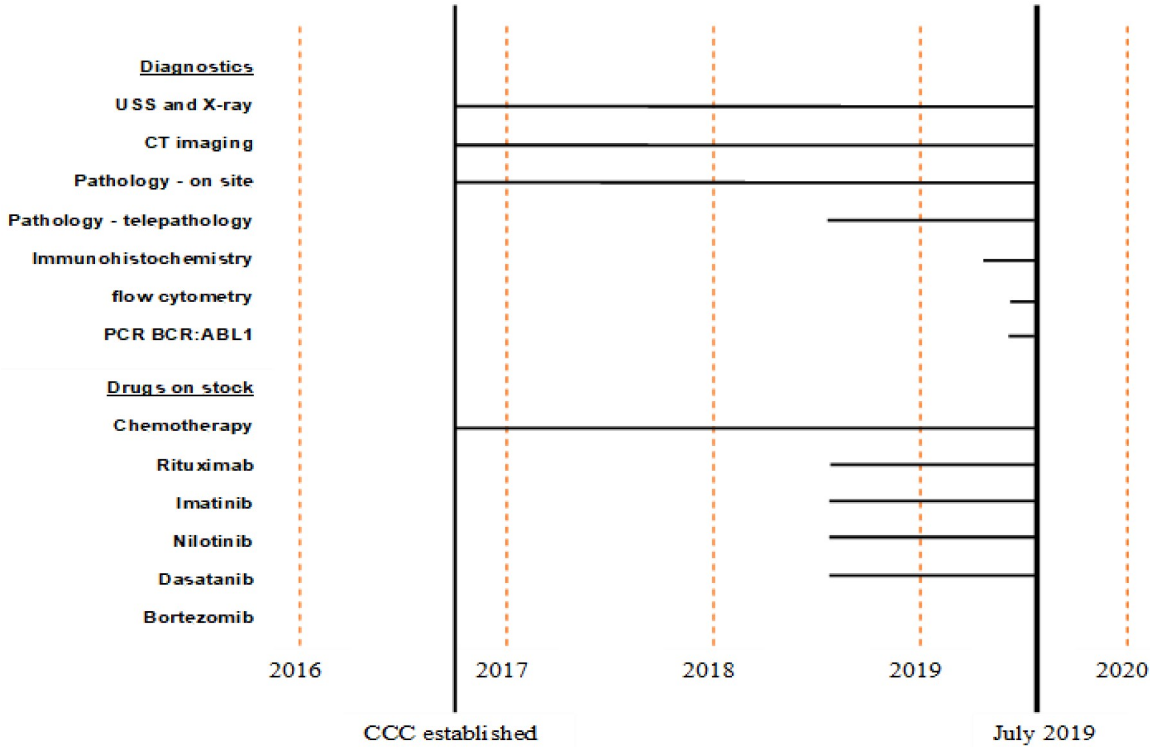

Fig 4. Diagnostics and medication on stock at the CCC since its establishment.

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reporting were likely contributing factors. Our data suggests that hematological malignancies are a significant problem within this East African population and are typically diagnosed at a younger age and at a later stage than in patients in high income settings. Additionally, Tanzania has one of the fastest growing populations and with this incidence will undoubtedly increase. Nonetheless, it is possible to establish a well-functioning hematology service within a low resource environment by using cooperation and already existing infrastructure.

Age at presentation

Average age at presentation in patients with MM, HL, CML and CLL were seen to be at least ten years lower than ages quoted by American and European literature. The median age for MM diagnosis in high resource settings is usually around 70 years of age with around 2% of cases occurring in those less than 40 years. In our cohort, median age at presentation was 58 years [7]. Similar figures have been documented in retrospective studies conducted in both Nigeria and Cameroon where median ages of 62 and 57 years have been quoted [8,9]. Interestingly however, in American cohorts although disease seems to be more aggressive in black patients, with shorter overall survival, no racial disparity was noted in age of onset [10,11].

A median age of 56 was recorded in patients with CLL in this cohort, which again compares to higher ages of 65–70 years in European and Northern American publications [12,13,14]. This younger age appears to correlate with an emerging pattern in African patients with average ages at onset of 56, 55 and 61 in Nigerian, Ethiopian and Senegalese cohorts respectively [15,16,17]. Unlike in MM however, younger age at presentation has also been reported in black patients in high income settings [18].

In CML, median age of 42 years was noted comparing to 66 in European and North American publications [12,13]. Again, similar trends are emerging, median age of 42 years at diagnosis was reported in a recent Senegalese cohort [19] and a mean difference of -7 years was seen between white and black patients in an American study [20].

Finally, in the case of Hodgkin lymphoma, same trends of earlier presentation have been seen in black patients and additionally a less apparent bimodal age distribution has been reported. Only the early peak in the 15–24 years old patients was observed in our cohort fitting with similar epidemiological data [21].

Although we can see that earlier age of onset does appear to be seen in black patients in high income settings in the case of CLL, CML and HL, these ages are still significantly higher than those reported in literature from Sub Saharan African cohorts [12,18,21]. Undoubtedly therefore genetics are likely to play a role, however environmental factors must be at play given the geographical disparity.

There are a number of possible explanations for these findings that have been proposed. Infection is likely to play a role with higher rates of HIV and EBV exposure affecting rates of lymphoma in younger patients [22]. There has also been a demonstrated link between multiple myeloma and EBV however impact on age of onset has not been determined [23]. In the case of our CLL patient population, the use of pesticides and artificial fertilizer might contribute to the number of CLL/SLL [24,25], taking into consideration that Kilimanjaro Region is known for a large use of pesticides [26], partly exceeding the WHO permissible limits, at least in the past [27]. However further research is required to evaluate the association between these factors and to identify other potential etiological causes.

Late stage presentation

Of interest is that these differences in age at presentation between high and low income settings are likely an undervaluation given the additional late stage at diagnosis also observed in this cohort. Late presentation has been well documented in the case of malignancies in low income settings [20]. Multiple factors have been suggested as contributing factors, including financial and geographical constraints. For patients living up to hundreds of kilometers from the center, or those experiencing financial burden, access to healthcare is limited [28]. In addition, lack of education about cancer amongst patients and health care workers as well [29,30] results in patients seeking health care elsewhere such as traditional healers, or the patients are misdiagnosed and treated incorrectly. For example, we experienced a lot of lymphoma cases that have been initially treated unsuccessfully for tuberculosis lymphadenitis for 6 months, before referral for biopsy consideration was made.

The median age at presentation is therefore estimated to be even younger if patients would present at a similar stage to those in high income settings. This is reflected in our cohort with 91% of HL cases and 81% of NHL cases presenting with Ann-Arbor stage 3 or 4 disease and 80% of all documented CLL cases presented in Binet stage C. Almost all patients with MM (93%) had bone lesions at time of diagnosis and hence presented in Salmon and Durie stage 3.

Diagnostics

Diagnosis and classification of hematological malignancy is becoming increasingly sophisticated as technology advances. This allows the development of new risk classifications and personalized medicine. But the costs of these diagnostics make their application in resource limited settings restricted.

Diagnosis at CCC is based on simple and cheap techniques ranging from morphology of the blood smear, bone marrow aspiration cytology, trephine histopathology and lymph node biopsies. The more expensive diagnostic means PCR and FACS was introduced by using existing infrastructure. This approach does not only lower capital costs, it avoids underutilization of the machines that lead to higher cost-per-test [31]. Furthermore, in the case of BCR-ABL PCR, it has reduced the costs for patients to 50% compared with the costs at private run laboratories and shortened the time to definitive diagnosis tremendously. Mendizabal et al. and Faye et al. reported about delays from diagnosis to treatment initiation, which can last more than 1 year due to financial constrains in paying for necessary diagnostic tests [32,33]. At CCC, the average time for definitive CML diagnosis is now less than 1 week.

Cooperating with international professional societies play a role in maintaining high quality results and for example telepathology gives (hemato-) pathologists an instant feedback on their findings and can contribute to quality assurance [34].

Apart from internal issues at the respective hospitals themselves, laboratory diagnostics in low resource settings face challenges like lack of reliable local or national vendors for quality reagents and consumables and slow and costly customs clearance process for international procurement [35,36] which leads to recurrent out of stock situations.

Treatment

Tanzania's National Health Insurance Fund (NHIF) covers most of the patient's chemotherapy treatment, including three antibodies (Rituximab, Trastuzumab and Bevacizumab), but the overall coverage is low, reaching only 7% of Tanzania´s population [37]. While the Community Health Fund covers 25% of the population, chemotherapies are not covered. Even though, through the governmental Medical Store Department, cancer medication can be obtained free of costs, procurement from this source of medication remains widely incomplete, hence CCC faces many out of stock situations. Therefore, deliveries through the private sector and donations through direct supply from DIFÄM, MAX Foundation and—for pediatric patients—from the Pediatric Department of the Muhimbili National Hospital (MNH), remain main sources.

The use of generic medicines and biosimilars should always be considered for cost savings and guidelines should be followed using the cheapest available medication, if applicable (e.g. starting Imatinib instead Nilotinib as first line treatment in CML patients).

For uninsured patients, the CCC social worker assesses the financial situation of each individual and obtains social support for those patients who cannot cover the cost of therapy, although this naturally cannot cover the more expensive treatments.

To date, CCC provides mostly the standard chemotherapy treatment regimens for hematological malignancies as first line treatments. Addition of Rituximab depends on drug availability, patient insurance status and financial ability of the patient. Second line treatments are also offered following international guidelines.

Despite increasing access to chemotherapies and monoclonal antibodies, challenges still persist. Transportation is a major limitation for many with some patients living up to two days drive from CCC. Hostel accommodation can be provided free of charge, however this requires complete relocation resulting in economic limitations for the patient and the greater family unit [38]. Even with patients living closer to the centre, limitations with infrastructure and transport particularly during rainy season can pose issues and often leads to delays or loss to follow up [38]. Similarly, for some patients, seeking urgent medical attention for example in the event of neutropenic fever is difficult, although this is hard to fully assess.

Management of the acute leukemias pose their own unique challenges. Delivering treatment often becomes unrealistic when considering barriers including blood product availability [39], patient isolation, broad spectrum antibiotic availability and the financial burden to uninsured patients. However, as the CCC expands and with plans in place for a dedicated oncology inpatient unit, many of these challenges will be mitigated. Induction therapies have been offered to AML patients, but infections during nadir pose an unsolved threat to date. Pediatric acute leukemias are referred to MNH as CCC is lacking a pediatric haemato-oncologist currently.

Limitations

It is likely a number of cases have not been registered in the cancer registry. Many of the acute leukemias for example are not treated due to factors described and often a formal diagnosis will not be made if death occurs early in admission due to the limited post-mortem service. Secondly, numbers for pediatric cases in particular are likely underrepresented due to direct referral to the Pediatric Department of MNH without passing through the CCC.

With regards to staging, what has been recognized is that in the early stage of the cancer registry recording of disease stage was sporadic and it has been difficult to chase paper files as the CCC moved to an electronic system. Ongoing advancements in the registration of cancer cases will lead to more accurate data in the future.

Conclusions

Hematological malignancies in Northern Tanzania occur generally at a younger age and a higher stage than in Europe or North America and it can be assumed that in particular infections play a key role herein.

Establishing services for the diagnosis and treatment of hematological malignancies in low income settings is not without its many challenges. However, the example of the establishment of the CCC at KCMC displays a way forward to close this service gap by utilizing and adapting existing infrastructures and machines, partnering with national and international organizations and universities. Data collection and accurate analysis will aid better understanding of hematological malignancies in the Tanzanian setting and allows better projecting and planning for future strategies to respond to the growing burden of hematological cancer diseases.

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Henke O, Mapendo PJ, Mkwizu EW, Lecoutre P. (2020) Early molecular response in East African Philadelphia chromosome positive chronic myeloid leukaemia patients treated with Imatinib and barriers to access treatment. *e*cancermedicalscience, 14:1091

Zielsetzung der Arbeit: In dieser Studie sollte das molekulare Ansprechen der Therapie mit dem TKI Imatinib bei neu diagnostizierten CML-Patientinnen und Patienten im KCMC nach drei Monaten als Prädiktor des Langzeitansprechens untersucht werden. Klinische Charakteristika, die mit einem schlechten molekularen Ansprechen korrelieren, sollten identifiziert und zudem Barrieren der Therapieadhärenz ermittelt werden.

Methoden und Ergebnisse: 30 therapieadhärente Patientinnen und Patienten konnten analysiert werden. Das mittlere Alter lag bei 41 Jahren. Der Medianwert der Leukozytenzahl lag bei 300/nl. Lediglich neun CML-Patientinnen erreichten ein gutes molekulares Ansprechen und in 16 Patienten wurde eine *complete haematologic response* gesehen. Während sämtliche Patienten eine Splenomegalie hatten, war die Hepatomegalie bei Diagnosestellung signifikant mit einem schlechten molekularen Ansprechen assoziiert. Andere signifikante Korrelationen konnten nicht ermittelt werden. Die üblichen CML-Risiko-Scores korrelierten nicht mit dem Ansprechen.
Mit im Mittel 282km vom Wohnort zum Behandlungszentrum stellen die Reisekosten und -zeit die größte Hürde für eine langfristige Therapieadhärenz dar.

Schlussfolgerungen: CML-Patienten waren im Schnitt jünger als Vergleichsgruppen im globalen Norden. Das Therapieansprechen entsprach nicht den Erwartungen, was vermutlich an einer späten Diagnosestellung und dem Vorliegen von aberranten genetischen Karyotypen liegt. Vermutlich sind in dem gegebenen Setting die üblichen Risiko-Scores nur bedingt zur Prädiktion des Therapieansprechens anwendbar. Weitere Studien mit Karyotypisierungen bzw. molekulargenetischen Untersuchungen von CML-Patienten aus Tansania bzw. SSA sind notwendig, um die Ergebnisse zu erklären. Die Ergebnisse fußen auf den Daten weniger Patientinnen und Patienten und sind daher mit Vorsicht zu interpretieren. Jedoch spiegeln sie im Kern die Ergebnisse aus anderen monozentrischen Studien in anderen afrikanischen Ländern wider.
Da ungeachtet der kostenlosen Medikation die Entfernung vom Wohnort zum Behandlungszentrum eine wichtige Barriere darstellt, können *Outreach Clinics* eine Alternative bieten.

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Early molecular response in East African Philadelphia chromosome-positive chronic myeloid leukaemia patients treated with Imatinib and barriers to access treatment

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Research

Abstract

Background: Data about haematologic malignancies from Tanzania are sparse. African studies show that chronic myeloid leukaemia (CML) is the most common leukaemia, and registry data display a lower mean age at diagnosis. Prognosis is generally good with tyrosine kinase inhibitors, but the molecular response of Imatinib treatment has never been studied in East Africa, and the outcome remains unknown. This study assessed the early molecular response (MR) as a predictor for long-term outcome and barriers to access treatment.

Methods: A case series of patients with CML from Northern Tanzania documented demographics and laboratory and clinical findings at diagnosis and after 3 months. The regression analysis has been performed on early MR and clinical and demographic variables using the χ^2-test. The barriers of potential treatments have been assessed.

Results: A total of 30 patients have been analysed. The mean age was 41 years. All patients had splenomegaly, whereas 16 had hepatomegaly. Complete haematologic response was achieved in 16 and early MR in 9 patients. Hepatomegaly was positively correlated with unfavourable early MR. The average kilometre from home to hospital was 282 km (5–1,158 km). Travel expenses and time investments pose an impediment to treatment.

Conclusion: Patients are younger, and early MR rates are lower compared to other studies. The finding of hepatomegaly as a risk factor for unfavourable early MR was described previously in West Africa. Adherence to therapy is high in the first months of treatment. Furthermore, research is needed to understand the poor MR and the common presentation of hepatomegaly. Outreach clinics might be a solution to reduce impediments to treatment.

Keywords: *chronic myeloid leukaemia, CML, Tanzania, molecular response, East Africa*

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Introduction

According to the Global Cancer Statistics, cancer becomes more of a global public health issue in low- and middle-income countries (LMICs) [1], due to multiple factors, e.g., increased life expectancy leading to the reduction of other causes of death, in addition to advances in diagnostic measurements and detection practices which contribute to higher cancer incidence [2].

For Tanzania, it is estimated that the cancer incidence will double by the year 2030, from 37,000 new cases in 2015 to more than 61,000 cases [3].

Global incidence of Chronic Myeloid Leukaemia

Chronic myeloid leukaemia (CML) is a haematologic malignancy and belongs to the group of myeloproliferative diseases. CML is the result of the chromosomal translocation t(9;22), which leads to a fusion gene between the *ABL1* proto-oncogene and the *BCR* gene [4]. The resulting product of this fusion gene is an active tyrosine kinase, leading to the uncontrolled proliferation of myeloid cell lineages [5] and, eventually, to leukaemia.

The crude annual incidence of CML in Europe ranges between 0.7 and 1.0/100,000 with a median age at a diagnosis of 57–60 years [6]. The data from the United States of America display an incidence rate of 1.6/100,000, and the WHO suggests that no association with race or ethnicity seems to exist [7]. However, due to the lack of reliable data for LMIC, the data for this part of the world remain an estimation [7], but taking the existing data for extrapolation, the worldwide incidence would be above 100,000 new cases each year.

A study from Sudan states that CML is the most common type of leukaemia in this country in patients with an age group of 16 years and above, whereas 'leukaemia' as a group of diseases is the second most common cancer entity in the country [8]. A retrospective data analysis from Ethiopia came to the same conclusion, as CML was the most common leukaemia entity amongst 67 cases of haematologic malignancies at a single centre [9]. CML as a very common entity in haematologic malignancies is also described for Libya in 2012 by Mehdi *et al* [10]. Remarkably, this study reports the fact that Black Africans are significantly more affected than non-Black Libyans.

Cancer data in Tanzania

At present, only three regional cancer registries in Tanzania exist at Ocean Road Cancer Institute (ORCI) in Dar Es Salaam (Coast Region), Bugando Medical Centre in Mwanza (Lake Region) and Kilimanjaro Christian Medical Centre (KCMC) in Moshi (Kilimanjaro Region). These databases rely mostly on diagnosis made by the respective pathology departments, and hence, haematologic malignancies that are diagnosed by other means such as polymerase chain reaction (PCR), karyotyping, flow cytometry and/or blood smear cytology are not documented. Before this background, the reliability of epidemiologic cancer data and malignant haematologic data, in particular, from Tanzania can be considered as weak as the data presented in the WHO country profile of Tanzania are incidence estimations based on the data of neighbouring countries [11].

Treatment

The treatment of CML patients changed fundamentally with the development of tyrosine kinase inhibitors (TKI). These drugs lead to greatly extended life expectancy which is now approaching that of the general population. On average, patients lose less than three life years due to CML if regular therapy is available [12]. Four drugs are currently available for the first-line therapy: Imatinib, Nilotinib, Dasatinib and Bosutinib. All of these TKIs are not only very effective but also expensive and a high economic burden for patients [13, 14] in low-resource settings, where healthcare coverage rate is low and out-of-pocket expenditures the norm.

In Tanzania, 3.5 million people are covered by the National Health Insurance Fund (NHIF) and 9.5 million by the Community Health Fund (CHF), which led to a coverage rate of 25% of the population in 2016 [15]. However, neither NHIF nor CHF covers any of the costs for TKI, and the latter does not cover specialised care such as haematologic consultations.

Through MAX foundation, a non-profit organisation in the United States of America, the programme 'Max Access Solutions' delivers free Imatinib (Nilotinib, Dasatinib and Ponatinib in the second-/third-line treatment) to partnering institutions in LMIC [16, 17]. This programme was open for patients only at ORCI until 2018 when KCMC Cancer Care Centre (CCC) became the second partnering hospital in Tanzania with a catchment area of 15 million people in the Northern part of the country and the first semi-urban partnering site of the programme worldwide.

Even though CML treatment is available in many LMICs through healthcare coverage or 'Max Access Solutions', the knowledge about patients' characteristics, prognosis, treatment response, adherence to therapy and obstacles to receive medications is limited or unknown for many countries, especially for East African countries.

This study should, therefore, serve two purposes: to display early molecular response to standard treatment with Imatinib as first-line therapy in newly diagnosed East African patients as a predictor for long-term outcome [18–20] and to explore obstacles for receiving treatment amongst these patients.

Methods

A consecutive case series study was performed on all patients with CML who were enrolled in the 'Max Access Programme' between August 2018 and November 2019 at KCMC. Data on demographics and laboratory and clinical findings have been obtained at the time of diagnosis and after 3 months of treatment with Imatinib. The complete haematological response (CHR) was defined according to the European Leukaemia Network (ELN): leucocytes $<10^9$/L, basophils <5%, no myelocytes, promyelocytes or blasts in the peripheral blood smear, thrombocytes $<450 \times 10^3/\mu$L and no palpable spleen [30]. The assessment of early molecular response is based on the international scale (IS) as the ratio of *BCR-ABL1* transcripts to *BCR1* transcripts and is expressed and reported as *BCR-ABL/ABL%* on a log scale, whereby results below 10% are considered as favourable molecular response (fMR) [30]. PCR was performed using 'GeneXpert® BCR-ABL Ultra' test from Cepheid®, a quantitative test for *BCR-ABL* major breakpoint (p210) transcripts.

The spleen size was measured from costal margin to the tip of the spleen using a measure tape, and the liver size was obtained by using ultrasound (Kaixin® DCU10) with linear measurements of the right liver lobe (maximum craniocaudal length) in the right medioclavicluar line.

Every patient was seen after 4 weeks for clinic visits and full blood counts, whereby treatment adherence was evaluated by asking the dosing schedule and how many capsules are left. PCR was repeated after 3 months of treatment.

At this time, every patient was asked about obstacles he/she faces with obtaining the treatment. Distance in kilometres from their home to the cancer care centre was determined by using Google Maps. The answers were recorded and categorised accordingly.

Regression analysis was performed on the 3 months molecular response and the clinical/demographic outcome by using χ^2-test and calculation of Fisher´s exact test for *p*-value, acknowledging the small sample size.

All patients gave informed consent to be enrolled into the Max Access Programme. They have been provided with both verbal and written information prior to Imatinib medication and PCR testing. Apart from the questions about barriers to treatment, all data gathered for this study were clinical routine data. Furthermore, written consent was given to use the data for research after explaining the purpose of the data collection, and an assurance was given that enrolment into Max Access Programme is unconditional of the consent of data collection. The continuation of treatment was secured through Max Access Programme.

Ethical clearance has been sought and granted by the Kilimanjaro Christian Medical University College, and ethical principals were applied according to the Declaration of Helsinki.

Results

In total, 34 patients have been diagnosed with CML between August 2018 and November 2019, of which two patients were lost to follow up after the first and the second months, respectively, and could not be evaluated for three early molecular responses. Another two patients were excluded from this analysis due to a treatment interruption of more than 5 subsequent days because of a temporary stockout of Imatinib.

All 30 analysed patients presented in chronic phase of the disease. Age, sex and laboratory results at diagnosis and 3 months are displayed for each patient in Table 1.

Table 1. Demographic and clinical variables at diagnosis (CHR and *BCR-ABL*/*ABL* ratio at 3 months).

No.	Age	Sex	WBC (10^9/L)*	Eosinophils in %	Basophils in %	Blasts in %	Hb (g/dL)*	Thrombocytes (10^3/µL)*	Hepatomegaly	*BCR-ABL*/*ABL* ratio*	*BCR-ABL*/*ABL* ratio at 3 months	CHR at 3 months
1	13	M	384	2	0	0	5.5	479	No	43%	0,63%	Yes
2	42	M	424	4	0	1	7.0	115	No	41%	15%	No
3	53	M	292	5	1	0	9.0	1004	No	23%	4.4%	Yes
4	40	M	366	1	7	0	10.5	320	Yes	58%	45%	No
5	53	M	180	0	1	0	7.2	293	No	100%	5.9%	Yes
6	4	M	499	9	1	0	6.9	198	Yes	67%	35%	No
7	60	F	322	4	0	1	8.7	150	No	56%	26%	Yes
8	36	M	374	3	0	0	5.8	806	Yes	43%	9.6%	Yes
9	31	F	300	0	2	0	13.2	351	No	45%	4.8%	Yes
10	42	M	264	2	1	0	9.8	502	Yes	58%	20%	Yes
11	41	M	225	3	0	2	7.9	309	No	29%	3.8%	Yes
12	50	M	280	5	0	0	8.3	240	Yes	61%	12%	No
13	53	M	390	7	0	0	7.3	398	Yes	14%	13%	Yes
14	30	F	260	5	2	3	9.9	440	Yes	74%	33%	No
15	42	F	78	2	0	4	9.8	278	No	120%	8.4%	Yes
16	54	M	388	1	0	2	8.4	618	Yes#	46%	38%	Yes
17	51	F	240	3	1	1	5.2	280	Yes	58%	83%	No
18	41	F	304	4	0	1	7.1	800	No	58%	12%	No
19	38	F	400	3	0	1	7.1	694	Yes	140%	110%	No
20	33	F	285	2	0	0	7.0	324	Yes	55%	24%	No
21	58	M	448	2	0	0	9.1	800	Yes	120%	78%	No
22	20	M	328	1	2	1	8.6	533	No	61%	44%	No
23	35	F	397	1	0	11	10.0	515	Yes	150%	38%	Yes
24	39	F	274	1	0	0	5.6	213	Yes	130%	30%	No
25	48	F	301	3	0	2	10.1	226	No	56%	3.1%	Yes
26	55	F	227	7	3	7	7.4	618	No	77%	0.57%	Yes
27	34	F	133	4	0	1	5.1	331	Yes	160%	13%	No
28	29	M	267	9	0	1	10.0	172	No	100%	19%	Yes
29	25	F	460	5	0	1	6.9	226	Yes	88%	13%	No
30	29	M	209	4	0	0	10.4	153	No	71%	26%	Yes

All patients had splenomegaly (#splenectomy due to splenomegaly before diagnosed with CML); all patients were diagnosed in chronic phase according to ELN criteria; WBC= white blood count; * at time of diagnosis; CHR = complete haematologic response; KM = kilometres; M = male; F = female.

Male:female ratio was 1.14, and the median age at diagnosis was 40.5 (4–60) years. The majority of patients worked as peasants (16), five patients were government employees, three patients were self-employed, two were students and four indicated other occupations. About 26 patients had an annual household income between 1 and 999 US-Dollar.

The median white blood count (WBC) was 300.5 × 10^9/L (78–499 × 10^9/L) and 327.5 × 10^3/µL (115–1004 × 10^3/µL) for thrombocytes, and half of the patients had at least 1% blasts in the peripheral smear at diagnosis. All patients presented with splenomegaly apart from one patient, who underwent splenectomy due to splenomegaly prior to diagnosis. Sixteen patients (53.3%) presented with hepatomegaly.

One patient was HIV positive and used antiretroviral therapy, and none of the patients was on treatment for tuberculosis during the study period.

CHR was achieved by 16 patients, whereas favourable early molecular response by 9 patients.

All patients adhered to the therapy with the dosage prescribed, and every patient was able to repeat the dosage scheme during all visits to the clinic. Missing days of medication occurred in four cases (three patients for 1 day and one patient for 3 days) due to belated attendance to the clinic.

The average kilometres from the patient's home to CCC were 282 km (5–1158 km). The most common reason mentioned as an impediment for treatment was travel expenses (n = 14), followed by time investment for travel (n = 13) and missing at work (n = 8).

Regression analysis (Table 2) showed that CHR significantly correlates with a favourable MR, whereas hepatomegaly is significant negatively correlated with it (Figure 1). Other clinical symptoms as well as sex, occupation and distance from home to hospital were not associated with the molecular outcome. Furthermore, there was no correlation found between the early molecular response results of the patients and the risk scores' classification of the population (Euro and Sokal, EUTOS and ELTS).

Discussion

The study was performed to determine the early molecular response amongst Tanzanian CML patients and impediments for treatment. To the best of authors' knowledge, this is the first study displaying early molecular response amongst CML patients treated with Imatinib in East Africa.

Demographics

The patients are on average younger than described in Europe and North America. The multicentre 'IRIS trial' included 1106 CML patients in chronic phase from Europe, North America and Oceania and reported a median age of 50 years [21]. The cohort had a median age of 39 years (41 years, respectively, if the two paediatric patients are excluded) and accords with data from 2013 from LMIC from 33,985 CML patients [22]. These data derive from the predecessor programme of 'Max Access Solution', so called 'The Glivec® International Patient Assistance Programme'. The findings state a mean average age of African patients of 39.5 years at the time of diagnosis. Only Asian patients were younger with an average mean age of 38.3 years. Across all the studies, men were more often affected than women, and the cohort shows a male/female ratio of 1:14. Mendizabal *et al* [9] stated, in a 2015 analysis of CML data from different regions in the world, that 'geographic and environmental heterogeneity suggest an important effect of environment'.

Another noticeable finding is the high WBC amongst the patients with an average of 309.9 × 10^9/L. The cohort of the IRIS study had a median WBC in both the study arms of 17.9 and 20.2, respectively. The finding of higher WBC in Sub-Saharan Africa has been described earlier [24–26] and is likely to be a sign of late presentation of the patients to the hospital. Following this logic, the late presentation contributes as well to the fact of splenomegaly in all patients in this study and in the majority of patients in other published African CML data [24,26,27,28].

Haematologic response

All patients responded to Imatinib therapy, and 53% achieved a CHR after 3 months of therapy according to the criteria of the ELN [29]. Achieving CHR was strongly correlated with an early favourable molecular response as half of these patients had a *BCR-ABL1* ratio ≤10%, whereas none of the patients without CHR achieved a favourable response. The achievement of only 53% is remarkably low if compared to data from ORCI in Dar Es Salaam, where a study reported 91% CHR after 3 months' treatment with Imatinib in 2016 [30]. However, the patients in the study from Dar Es Salaam had lower WBC at the time of diagnosis. One can assume that patients in Dar Es Salaam, a metropolitan area, present earlier to the hospital due to the better availability of health services. Similar findings were published from Dakar in Senegal with 82.4% CHR [25].

Table 2. regression analysis of clinical and sociodemographic variables.

Variable	***n***	**fMR at 3 months *n* (%)**	**ufMR at 3 months *n* (%)**	***p*-value (Fisher´s exact test)**
All patients	30	9 (30)	21 (70)	
Mean age in years at Diagnosis	39.2			
Gender				
• Male	16	5 (31.3)	11 (68.7)	1.00000 OR 1.13636 (0.18298–7.16311)
• Female	14	4 (28.6)	10 (71.4)	
Employment				
• Agriculture	16	6 (37.5)	10 (62.5)	0.43972 OR 2.20000 (0.33914–15.37130)
• Other	14	3 (21.4)	11 (78.2)	
Kilometres from home to hospital				
• > 30 km	25	7 (28)	18 (72)	0.62202
• > 85 km	14	3 (21)	11 (79)	0.43972
• > 100 km	12	3 (25)	9 (75)	0.70356
Complete haematological response				
• yes	16	9 (56.3)	7 (43.7)	**0.00094** OR 0.00272 (0.00004–0.39724)
• no	14	0 (0)	14 (100)	
Clinical symptoms at Dx				
• Splenomegaly	$30^{\#}$	-	-	-
• Hepatomegaly	16	1 (6,3)	15 (93,8)	**0.0043** OR 0.05000 (0.00190–0.57664)
• Skin nodules	4	1 (25)	3 (75)	1.00000
• Fatigue	13	4 (30.7)	9 (69.3)	1.00000
• Blasts >1% in peripheral smear	15	4 (26.7)	11 (73.3)	1.00000
• Hearing loss/impairment	5	2 (40)	3 (60)	1.00000

fMR = favourable early molecular response (bcr–abl/abl <10%); ufMR = unfavourable early molecular response (*BCR-ABL/ABL* > 10%); ($^{\#}$1 patient with splenectomy due to splenomegaly before diagnosed with CML)

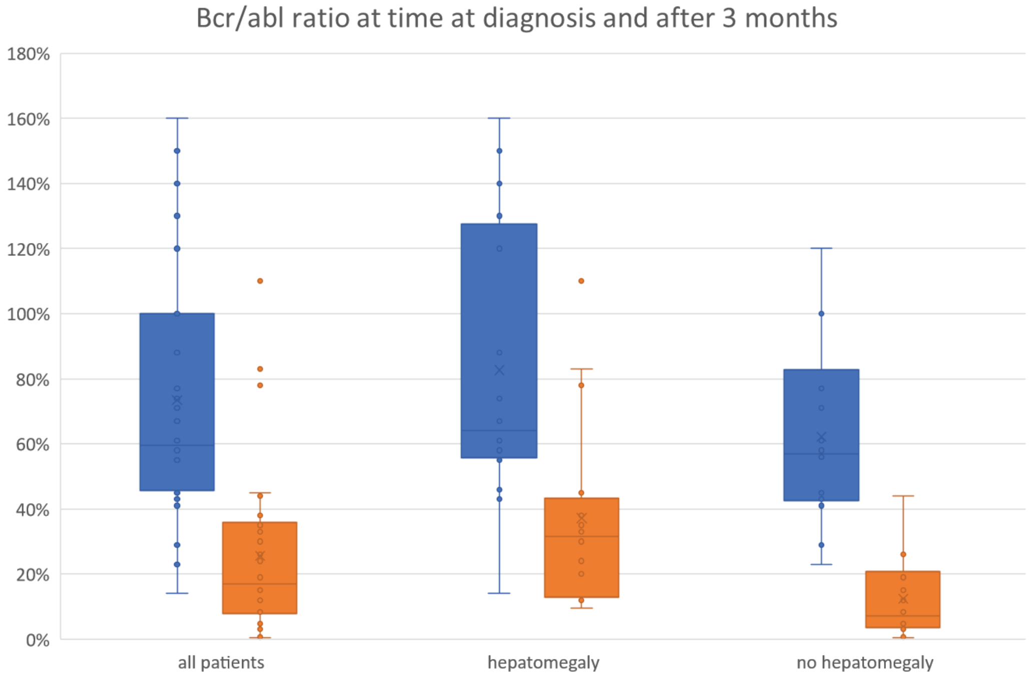

Figure 1. ***BCR-ABL/ABL*** **ratio at the time of diagnosis and after 3 months of treatment (all patients and by patients with and without hepatomegaly).**

Early molecular response

The early molecular response rate at 3 months can be described as low with only 30% of patients achieving a *BCR-ABL/ABL* ratio ≤10%. On the contrary, the German cohort from the previously cited IRIS study showed that 74.5% (out of 51 patients) achieved a ratio of ≤1% at 3 months of treatment with Imatinib [31], and a recent published study from China stated that 55.7% of 79 patients achieved ≤10% with Imatinib [30]. Adherence to therapy in this study has been secured in all patients, and a significant reduction of WBC, reduction or diminishing of splenomegaly was seen in all the patients. However, an uncertainty remains in the interpretation of the chronic phase (CP) of this cohort. According to the ELN criteria [8], all 30 patients were in CP at the time of diagnosis, but given the fact that no karyotyping was performed—due to the lack of this technique in the routine diagnostic in Tanzania—and additional chromosomal aberrations at diagnosis define the accelerated phase according to the WHO [10]. One could speculate that some patients of this cohort were underdosed with Imatinib and, hence, achieved a poor outcome. Koffi *et al* [28] discovered additional cytogenetic aberrations in 41% of 42 newly diagnosed CML patients from Ivory Coast in 2010. Another interpretation refers to the pharmacokinetics of Imatinib. A study of 126 Nigerian patients [33] revealed that the clearance of Imatinib differs significantly from other publications in different regions of the world, and the authors concluded that this might contribute to the poorer outcome as well. These interpretations, however, remain uncertain amongst East African patients as long as no further studies are conducted to proof these hypotheses.

Hepatomegaly

From all clinical variables, only hepatomegaly was found to be associated with an unfavourable early molecular response. This finding is in line with other studies from Ivory Coast [26] and Nigeria [34], suggesting that hepatomegaly has a prognostic validity toward worse treatment outcome (significantly reduced overall survival). Furthermore, the study from Dar Es Salaam that described a high CHR of 91% amongst their cohort [30] had only 22.8% of patients with hepatomegaly, whereas, in this cohort, 56.7% had an enlarged liver.

A European study identified hepatomegaly as an adverse predictor of treatment failure: Lekovic et al. analysed 168 CML patients in CP from Serbia and found leucocytosis >100,000 × 10^9/L, blasts in peripheral blood ≥1%, presence of additional cytogenetic aberrations and hepatomegaly as risk factors for treatment failure [35]. On these findings, the authors developed a prognosis score which correlated better with the treatment outcome of their cohort than the Sokal-, Hasford- and EUTOS-Scores.

Astonishingly, a historic article published in 1978 [36] stated that liver volume has a prognostic value in CML, and furthermore, the hypothesis was discussed that extramedullary haemopoiesis—as the cause of hepatomegaly—in the liver may play an important role in clonal evolution of CML towards a blastic transformation as the authors stated back then. Yet a hypothesis, but a possible explanation for the clinical findings of the previous studies.

Impediments to treatment

Barriers to accessing treatment in low-resource settings have been researched and published in the last years. A recent qualitative study from Kenya [37] identified the following reasons amongst cancer patients: High costs of testing and treatment, low level of knowledge about cancer in both patients and clinicians, long distances to access diagnostic and treatment and poor communication. CML patients at CCC have the possibility to get a full or partial exemption from diagnostic tests (blood counts, biochemistry and PCR), and the TKI is free of charge through the MAX Access Programme. Apart from these facts, there are still difficulties for the patients. Attendance to the clinics on a regular basis is challenging mostly due to long travel distances and travel fares. The average distance in kilometres from the patient's home to CCC was 282 km, whereas some patients need to travel more than 1,000 km to have access to TKI. Besides the fare for the travel itself, the necessity to stay overnight before returning to their homes implies further costs. Most of the patients are peasants, and being away from home is tantamount to leave the field and crops unattended. Impassable roads during the rainy season are another challenge for patients to attend on a regular basis. However, the distance has no influence on the early molecular response, which might change during the following years of treatment.

A possible solution is to bring the service to the patients and not vice versa. The 'Hub and Spoke Model' [38–40] is an example, whereby a leading centre will supervise smaller health facilities in rural areas for treatment and follow-up of (cancer) patients. Cases needing more attention and sophisticated diagnostic will be referred to the 'hub'. In CML patients, who are treated with oral medication, this model might be very eligible. It would lead to patients having to visit the leading centre for initial diagnosis and 'milestones' during follow-up only, whereas regular clinical and simple laboratory examination and medication refill can be conducted near their homes. In particular, in a territorial state with weak transport infrastructure, it seems to be promising.

Limitations

The result will not be representative for the population in Tanzania. The location of the hospital will lead to a bias towards urban populations. This bias will be accentuated during the rainy season when patients from rural areas cannot reach the hospital due to impassable roads. Access to KCMC is limited to people with health insurance or financial possibilities to afford expenses for consultation and/or admission. This might lead to the exclusion of many people with a low economic background.

The small sample of patients must be taken into consideration when interpreting the results.

Conclusions

Imatinib treatment in a semi-urban setting in East Africa is effective; however, the early molecular response amongst the patients is lower than reported in high-income countries. Further studies are needed to explain the low response rate to Imatinib. The role of hepatomegaly as an adverse clinical feature needs to be examined further, especially with regards to extramedullary haematopoiesis and genetic aberrations. The latter might be useful for an adapted African prognosis score and treatment decision-making.

Patients from low-resource countries still face massive barriers despite free treatment and diagnostics. Bringing treatment to the patients—especially in rural areas—might be the key to ensuring good treatment adherence and outcome.

Conflicts of interest

The authors declare no conflicts of interest.

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4. Diskussion

Ausbildung, Gesundheitskompetenz und Personal

Die oben dargestellten Forschungsarbeiten beschäftigen sich mit unterschiedlichen Aspekten, die im Kontext der Thematik der onkologischen Versorgung in ressourcenarmen Ländern wichtige Rollen einnehmen. Drei der sechs Originalarbeiten widmen sich dem Themenkomplex der Gesundheitskompetenz in Tansania, sowohl von der Allgemeinbevölkerung, von Patientinnen und Patienten als auch von Gesundheitsdienstleistern. Zwei weitere Arbeiten fokussieren auf klinische Aspekte der onkologischen Versorgung und eine Publikation auf Herausforderungen im Aufbau von Krebsbehandlungseinheiten.

Dabei gibt es in allen Aspekten Überschneidungen und Themen, die sich gegenseitig beeinflussen. Die Gesamtbetrachtung der hier vorgelegten Forschungsarbeiten stellt somit auch ein Beispiel für die Interdisziplinarität von Global Health dar, die durch die Verbindung von klinischen und angrenzenden gesundheitswissenschaftlichen Themenfeldern gekennzeichnet ist. Im Folgenden sind die wichtigsten Ergebnisse der Arbeiten zusammengefasst.

In der Studie *„Use of Herbal Medicine Is Associated with Late-Stage Presentation in Tanzanian Patients With Cancer: A Survey to Assess the Utilization of and Reasons for the Use of Herbal Medicine”* (Henke et al., 2022a) stellen wir erstmals in Tansania den Zusammenhang zwischen der in der Einleitung erwähnten *late stage presentation* von Krebspatienten und der weit verbreiteten Nutzung der Naturheilkunde dar. Für Patientinnen und Patienten im Erkrankungsstadium IV bei Erstdiagnose konnten wir eine signifikante Korrelation zur *vorherigen* Anwendung (d.h. vor der Nutzung konventioneller Medizin) von naturheilkundlichen Maßnahmen aufzeigen. Wir interpretieren dies als Ausdruck der Verzögerung von Diagnostik und des Therapiebeginn durch den Glauben an die Wirkung der naturheilkundlichen Medizin und damit deren Nutzung. Diese Annahme wird unterstützt durch Publikationen aus Malaysia (Mohd Mujar et al., 2017), Indien (Broom et al., 2009) und Südafrika (Cacala und Gilart, 2017). Wenngleich in diesen Arbeiten keine direkte Korrelation zu den Krankheitsstadien hergestellt wurde, so wurde jedoch die Nutzung alternativer Medizin als Faktor für die Verzögerung der Diagnostik identifiziert. Dabei spielt der Glaube an eine Heilung einzig durch Naturheilkunde eine größere Rolle als das Fehlen konventioneller onkologischer Angebote in der Nähe des Wohnortes der Erkrankten. Dieses fehlende Vertrauen in die Schulmedizin spiegelt sich auch in der Publikation von Rick et al. (Rick T et al., 2021) wider, die im KCMC die Gründe für eine verzögerte Diagnosestellung unter Krebspatienten untersuchten. *„I don´t think the problem could be cured by medicine”* war neben *“I had seen or heard of other people not be cured”* eine häufige Aussage der Befragten. Traditionen spielen im Umgang mit Krankheit in Tansania eine entscheidende Rolle, diese sind dabei nicht per se „anti-modern“, sondern tief verwurzelt mit der Art und Weise Unglück und Krankheit zu erklären (Langwick, 2011). So erläuterten auch viele unserer Befragten ihre Entscheidung mit *„due to tradition“*. Wir schlussfolgern, dass den Missverständnissen über schulmedizinische Konzepte durch vermehrte Gesundheitsaufklärung und -erziehung begegnet werden muss, und dies ein entscheidender Baustein dafür ist, *late stage presentation* zu begegnen.

Dass Gesundheitsaufklärung und -erziehung notwendig sind, zeigt sich auch in den Ergebnissen der zweiten hier dargestellten Studie. In *„Tanzanian women´s knowledge about Cervical Cancer and HPV and their Prevalence of positive VIA cervical screening results. Data from a Prevention and Awareness Campaign in Northern Tanzania, 2017 – 2019”* (Henke et al., 2021) kannten nur 22% der Befragten aus der Allgemeinbevölkerung den Begriff „Gebärmutterhalskrebs“ – der häufigsten Krebserkrankung in Tansania. Nur 25% hatten schon einmal von einer HPV-Infektion gehört. Dabei korrelierte das Wissen jeweils mit einem höheren Einkommen und der Teilnahme an Screening-Programmen. Unerwartet war die fehlende Korrelation zu Bildung, was sich durch die die in den Jahren zuvor durchgeführten staatlichen Gebärmutterhals-Vorsorgeprogramme erklären könnte, denen landesweit große Aufmerksamkeit durch Medienkampagnen geschenkt wurde (Moshi et al., 2018). Hier wurden, so die Schlussfolgerung, große Teile der Bevölkerung unabhängig von ihrem Bildungsstatus erreicht. Insgesamt konnten wir in dieser Befragung von 2192 interviewten Teilnehmenden jedoch ein höheres Wissen um Zervixkarzinome und HPV aufzeigen als in Studien in anderen Landesteilen Tansanias (Mabelele et al., 2018, Moshi et al., 2018). Wir interpretieren dies mit der vergleichsweise guten Abdeckung mit Gesundheitsdienstleistern in der Kilimanjaro Region. Dort herrscht, nach der Metropolregion Dar Es Salaam, die höchste Dichte an Gesundheitseinrichtungen (MoHSW, 2008) in Tansania. Dies spiegelt sich auch in der positiven Korrelation von

Wissen und Vorhandensein einer Krankenversicherung und damit einem niedrigschwelligen Zugang zu Gesundheitseinrichtungen unter den Befragten wider. Folgerichtig war auch der Anteil an HIV- und VIA-Positivität unter den 2224 Frauen, die am Gebärmutterhalsscreening teilnahmen, mit 2,6% und 3,1%, geringer als in anderen Studien aus Tansania. Wenngleich die Ergebnisse eine höhere Gesundheitskompetenz in der Kilimanjaro Region auszuweisen scheinen, so ist sie dennoch unzureichend, um das von der WHO ausgegebene Ziel „90-70-90“ (WHO, 2020) bis 2030 zu erreichen: 90% der Mädchen bis 15 Jahre sind gegen HPV geimpft, 70% der Frauen sind im Alter von 35 und 45 Jahren gescreent und 90% der Frauen mit Präkanzerosen und invasivem Zervixkarzinom werden behandelt. Aufklärungskampagnen können hier die Situation verbessern helfen und die Einbindung von primären Gesundheitseinrichtungen in die Krebsaufklärung und -vorsorge dürfte einen positiven Einfluss auf die Gesundheitskompetenz der Menschen haben.

Die dritte Studie fokussiert auf die Mitarbeitenden aus den primären Gesundheitseinrichtungen und untersucht den Einfluss von gezielten Ein-Tages-Trainings, durchgeführt durch Mitarbeitende des KCMC, über Krebs auf die Mitarbeitenden selbst und ihre Arbeit in den Gemeinden (Singer et al., 2019). Dabei konnte unsere Intervention zeigen, dass ein eintägiger Kurs bei 41 Mitarbeitern des primären Gesundheitssektors zu einem signifikanten Anstieg des Wissens beitrug und nach Wiederholung des Kurses ein weiterer Lernzuwachs zu beobachten war, der auch nach drei Monaten noch bestand hatte. Eine Studie von Rick et al. (Rick et al., 2019) konnte ebenfalls einen Wissenszuwachs über Mamma- und Zerivxkarzinome bei *„frontline health care workers“* nach einem eintägigen Kurs beobachten, fokussierte jedoch nicht auf *„community* und *dispensary health care workers“* (CHW) wie in unserer Studie, sondern auf Ärzte, *Clinical Officers* und Pflegende. Mit dem Fokus auf CHW als unmittelbaren und in der Regel ersten Kontakt zu den Erkrankten, folgen wir den Empfehlungen der WHO zur Integration von CHW in die Forschung, um die SDG zu erreichen (Maher und Cometto, 2016). Mit diesem Schwerpunkt konnte die Studie erstmals in Tansania die Auswirkungen auf die Krebsaufklärungsarbeit in den Gemeinden der CHW mittels qualitativer Methoden (Fokusgruppen-Diskussion) darstellen. Dabei zeigte sich, dass das Training insbesondere die Selbstsicherheit der CHW im Umgang mit Krebserkrankungen stärken konnte und so zu einer besseren

Aufklärung der Menschen in ihren Gemeinden beitragen sowie Irrglaube und Erwartungen an alternative Heilmethoden besser einordnen helfen konnte. Zudem fungieren sie als wichtige Verbindung zwischen primärem Gesundheitssektor und der tertiären Ebene, durch direkte Kommunikation und Anbindung von Krebsverdachtsfällen. Letzteres kann einen wichtigen Beitrag zur Reduzierung der *late stage presentation* bieten, da fehlende Kommunikation zwischen den Gesundheitseinrichtungen einen wichtigen Risikofaktor hierfür darstellt (Kwesigabo et al., 2012). Eine entscheidende Erkenntnis dieser Studie ist zudem, dass das Ein-Tage-Training einen nachhaltigen Effekt aufweist und kostengünstig durchzuführen ist. Durch die Kürze der Intervention ist die Routineversorgung der Bevölkerung nur sehr begrenzt beeinflusst, was bei anderen Interventionen in LMIC oft ein Problem darstellen kann (Gallagher et al., 2018) bis hin zur Verschlechterung der Gesundheitsdienstleistungen (Deserranno et al., 2020; Barber und Bowie, 2008).
Wir schlussfolgern aus den Ergebnissen, dass CHW einen entscheidenden Beitrag zur *cancer control strategy* in Tansania liefern können.

Die vierte Arbeit beschäftigt sich mit den Herausforderungen im Aufbau einer Onkologischen Abteilung in einem tertiären Krankenhaus. Eine wissenschaftliche Untersuchung der Sichtweisen unterschiedlicher Akteure in diesem Prozess wurde in SSA bislang nicht untersucht, kann aber wichtige Aspekte liefern, die bei der Etablierung von Krebsbehandlungseinrichtungen hilfreich sein können. In offenen Interviews von Ärztinnen und Ärzten, Krankenschwestern, Apotheker und Mitarbeitern der Administration wurden die Themen „Training und Weiterbildung, Verfügbarkeit finanzieller Mittel, Managementherausforderungen, zukünftige Entwicklung und Berufszufriedenheit“ (Alwash et al,. 2019) als wichtige Aspekte im Aufbau identifiziert. Die Ergebnisse spiegeln erneut die mangelhafte Ausbildung in der Onkologie wider, die in anderen Studien in Tansania festgestellt wurden (Makani et al., 2017; Rick et al., 2019; Urasa et al., 2011). Darüber hinaus konnten wir feststellen, nach unserem Wissen erstmalig in SSA, dass die unzureichende Ausbildung mit Ängsten beim Personal verbunden ist, insbesondere, wenn es um den Umgang mit Zytostatika geht: *„Most of the time you are giving it [chemotherapy] you are not at peace at it. What if something goes wrong, what if I start getting the effect?”* und *“I am worried of the leakage of chemotherapy, my worry is suffering later in the future, so we need more protective gear”.* Diese Ängste können durch den Mangel an persönlicher

Schutzausrüstung zusätzlich verstärkt werden (Easty et al., 2015), was sich in dieser Aussage ausdrückt: *„I feel well and protected but sometimes you´re missing some of the PPE [personal protective equipment], sometimes maybe the mask is over, there is no replacement; the google is over, there is no replacement. But when we have those, I feel like protected.”*

Die Studienteilnehmer drücken den Wunsch nach mehr Training und Ausbildung in fast allen Interviews aus (*„Bottom line is supervision and the need to train people.*“), was den Kreis zu den vorherigen Arbeiten und den Problemen mangelnder Gesundheitskompetenz schließt.

Ein weiterer wichtiger Aspekt war der Wunsch nach finanzieller Nachhaltigkeit der eignen Einrichtung und Ängste vor einer finanziellen Abhängigkeit von einer Vielzahl internationaler Organisationen. Die Teilnehmenden der Interviews fordern dabei mehr Engagement von der eigenen Gesundheitspolitik: *„We need to act fast and try and get the government involved and support as much as I can to make the medications even available in our country.”* und *“When we are trying to ask the patient to contribute to that they say that cancer patients have to get free treatment that´s the word that they hear from the government while we don´t have any money form the government or any drugs from the government. Now, all chemotherapy from the government has been allocated into the Ocean Road but maybe this year we may get some.”.*

Die Lancet Oncology Commission hat 2022 in ihrer Publikation „Cancer in Sub-Saharan Africa: a Lancet Oncology Commission” (Ngwa et al., 2022) u.a. auch eine verlässliche und planbare Medikamentenversorgung von den nationalen Regierungen in SSA gefordert.

Klinische Aspekte

Die beiden folgenden Arbeiten fokussieren auf die klinischen Charakteristika von Patientinnen und Patienten mit malignen hämatologischen Erkrankungen und die Behandlungsergebnisse bei Chronisch Myeloischer Leukämie (CML).

In der Publikation *“Hematological Malignancies in East Africa – Which cancers to expect and how to provide services.”* (Leak et al., 2020) wird zudem der Aufbau des hämato-onkologischen Behandlungsangebots in dem ressourcenarmen Land Tansania beschrieben, neben einer retrospektiven Analyse aller Krankenakten von Patientinnen und Patienten mit hämatologischen Neoplasien von Eröffnung des

Cancer Care Centre im Dezember 2016 bis Mai 2019. Wichtigste Erkenntnisse dieser Querschnittsanalyse sind zum einen das jüngere Durchschnittsalter der Erkrankten bei Erstdiagnose verglichen mit Daten aus HIC und der fehlende bimodale Altersgipfel (Grotmol et al., 2011) unter den Hodgkin Lymphom Patienten. Letzteres wurde von Shenoy et al. (Shenoy et al., 2011) ebenfalls bei afroamerikanischen Patienten in den USA beschrieben, es sind jedoch keine weiteren Studien aus SSA hierüber veröffentlicht worden, um dieses Ergebnis in einen innerafrikanischen Kontext zu setzen. Im Gegensatz hierzu ist der um zehn Jahre geringere Altersdurchschnitt bei Erstdiagnose eines Multiplen Myeloms und der CML mit Publikationen aus SSA im Einklang: Unsere Patientinnen und Patienten mit Multiplem Myelom waren durchschnittlich 58 Jahre alt, in Nigeria und Kamerun 62 bzw. 57 Jahre (Odunukwe et al., 2015; Dongho et al., 2018). Äthiopische und tansanische CML-Patienten waren mit durchschnittlich 33 und 45 Jahren (Tadesse et al., 2021; Nasser et al., 2021) deutlich jünger als europäische und nordamerikanische Patientinnen und Patienten mit 57 Jahren (Hochhaus et al., 2020).
Bemerkenswert dabei ist, dass ein Altersunterschied bei Patientinnen und Patienten mit Multiplem Myelom bei Erstdiagnose in den USA zwischen afroamerikanischen und kaukasischen US-Amerikanern nicht festgestellt wurde (Kennedey-LeJeune et al., 2018; Banavali et al., 2018), für die CML konnte dies jedoch beschrieben werden (Robbins et al., 2015). Wenngleich sich hier Muster in der Epidemiologie zwischen den Ethnien abzeichnen, so sind die Altersunterscheide in den Kohorten aus SSA dennoch signifikant höher als in den inter-ethnischen Kohorten aus HIC, was uns schlussfolgern lässt, dass neben genetischen Unterschieden insbesondere Umwelteinflüsse einen großen Einfluss haben, betrachtet man die geographischen Unterschiede.

Die zweite Publikation, die sich mit hämatologischen Neoplasien beschäftigt, ist *„Early molecular response in East African Philadelphia chromosome-positive chronic myeloid leukaemia patients treated with Imatinib and barriers to access treatment"* (Henke et al., 2020). In dieser prospektiven Studie sollte das Ansprechen von CML-Patientinnen und Patienten auf die Therapie mit dem Tyrosin-Kinase-Inhibitor (TKI) Imatinib (als verfügbare Standardtherapie in Tansania) untersucht werden. Hintergrund dieser Arbeit waren eigene Beobachtungen und wenige klinischen Studien aus SSA, die ein schlechteres Therapieansprechen auf Imatinib aufzeigen konnten als dies durch die Datenlage aus HIC zu erwarten wäre (Tapela et al., 2018; Faye et al., 2016; Gaudong et al., 2016). Das frühe molekulare Ansprechen (*early molecular response*) diente in dieser Studie als Prädiktor für eine Langzeitremission (Hanfstein et al., 2012) und war die erste publizierte Studie in Ostafrika, die das molekulare Ansprechen untersuchte. Zusätzlich stellten wir sicher, dass nur Patientinnen und Patienten in die Analyse eingeschlossen wurde, die eine ausreichende Therapieadhärenz nach drei Monaten aufweisen konnten. Wir stellten fest, dass sowohl die *complete haematological response* als auch die *favourable molecular response* als Marker für das Therapieansprechen gemäß der Leitlinie des *European Leukaemia Network* (Hochhaus et al., 2020) nur von 53% bzw. 30% der Behandelten erreicht wurde. Die *favourable molecular response* war dabei positiv korreliert mit Erreichen der *complete haematological response*, was erwartbar war, und negativ mit dem Vorliegen einer Hepatomegalie. Letzteres wurde sowohl 2008 und 2010 in der Côte d´Ivore beschrieben (Nanho et al., 2008; Koffi et al., 2010) und 2017 von Lekovic et al. in Serbien als Prädiktor eines Imatinib-Therapieversagens (Lekovic et al. 2017) identifiziert. In dieser retrospektiven Analyse aus Serbien korrelierten Hepatomegalie, Leukozytose >100/nl, Blasten ≥1% und *additional cytogenetic aberrations* besser mit dem Therapieansprechen als die etablierten CML-Prognose-Scores (EUTOS, Sokal, Hasford), die auch in unserer Kohorte nicht mit dem molekularen Ansprechen korrelierten. Wir schlussfolgern aus den Ergebnissen, dass das Therapieansprechen unserer Patientinnen und Patienten schlechter ist als in HIC und vermuteten das Vorliegen von *additional cytogenetic aberrations* als Grund dafür, deren Nachweis in der Routinediagnostik in Tansania nicht verfügbar sind. Dies konnten wir später in einer kleineren Kohorte von tansanischen CML-Patientinnen und Patienten nachweisen (Henke et al., 2021) und konnte ebenso von Tadesse et al. aus Äthiopien, die das Spektrum der BCR-ABL-Mutationen ihrer Patienten untersuchten (Tadesse et al., 2021), aufgezeigt werden. Weiterhin folgerten wir, dass die in HIC etablierten Prognose-Scores in SSA wahrscheinlich keine akkuraten Vorhersagen treffen können, was auch mit der *late stage presentation* und dem damit einhergehenden Erwerb weiterer zytogenetischer Aberrationen über die Zeit geschuldet sein könnte. Eine *late stage presentation* der Patienten ist anzunehmen, da die durchschnittliche Leukozytose bei 300/nl lag und alle Patienten eine Splenomegalie zum Zeitpunkt der Erstdiagnose aufwiesen. Ein adaptierter Prognose-Score, der die verfügbaren Routinediagnostik in SSA berücksichtigt, wäre sinnvoll und wünschenswert, um bessere Therapieergebnisse zu erzielen.

5. Zusammenfassung

Onkologische Vorsorge, Diagnostik und Behandlung in Ländern mit niedrigem und mittlerem Einkommen ist in vielen Aspekten komplex, aber die Beschäftigung damit dringend geboten vor dem Hintergrund der rapide steigenden Krebsinzidenz in diesen Ländern.

Abb. 6 versucht die unterschiedlichen Akteure und Themen von *Global Oncology* in einer Mindmap darzustellen und ist das Ergebnis eines Workshops internationaler Fachkräfte auf diesem Gebiet (Henke et al., 2023)

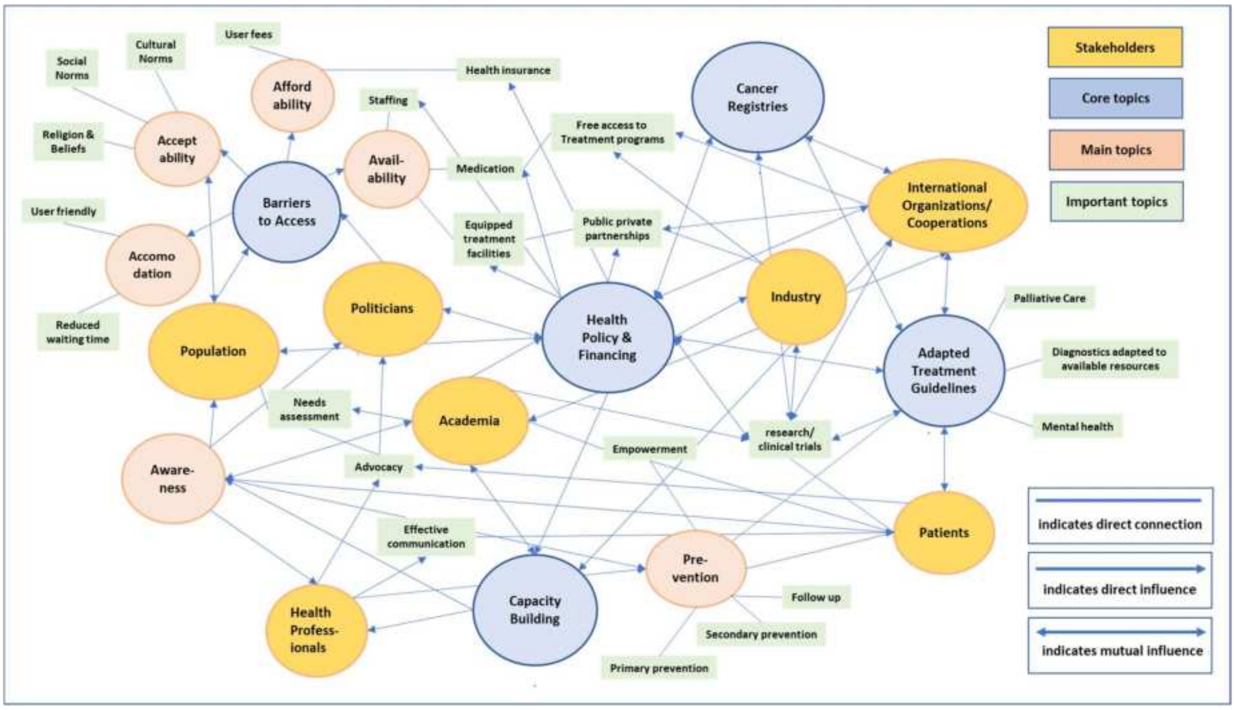

Abb. 6: Mind-mapping der komplexen Thematik der Onkologie in LMIC. Ergebnis eines Workshops internationaler Teilnehmer der 1st International Hospital Partnership Conference der Gesellschaft für Internationale Zusammenarbeit (GIZ) (Henke et al., 2023)

Die in dieser Habilitationsschrift dargestellten wissenschaftlichen Originalarbeiten leisten einen Beitrag zum besseren Verstehen der Thematik und können als Grundlage für weitere wissenschaftliche und praktische Arbeiten, insbesondere in SSA, dienen.

Als übergreifendes Thema aller hier dargestellten Publikationen kann die fehlende bzw. mangelnde Gesundheitskompetenz der Bevölkerung in Tansania genannt werden, die sowohl auf Behandlerseite, aber auch auf Patientenseite besteht und über unterschiedliche Mechanismen zur *late stage presentation* führt, die in LMIC für die hohe Krebsmortalität verantwortlich ist. Eine Stärkung der Gesundheitskompetenz durch Aufklärungs- und Vorsorgekampagnen, vermehrte Ausbildung von onkologischem Fachpersonal, aber auch bessere Integration onkologischer Themen in die bestehenden Curricula von Gesundheitsmitarbeitenden bieten Lösungsansätze.

Daneben muss jedoch auch festgestellt werden, dass das Wissen um onkologische Erkrankungen in LMIC, mit ihren regionalen ethnischen, kulturellen und genetischen Unterschieden sowie den Umwelteinflüssen in weiten Teilen bis dato unverstanden ist. Therapiekonzepte aus HIC lassen sich nicht ohne Weiteres auf LMIC übertragen und intensivierte Forschungen, insbesondere im Bereich der personalisierten Medizin (*precision oncology*), sind notwendig, um in den Ländern des globalen Südens effektive Konzepte und Strategien gegen die hohe Mortalität und Morbidität einzuführen. Da Krebspatientinnen und -patienten in LMIC durchschnittlich jünger sind als in HIC und damit häufig die Ernährer der Familien betroffen sind, trägt eine verbesserte onkologische Versorgung in LMIC auch zur Reduzierung der Armut im globalen Süden bei.

6. Überlappung durch geteilte Autorenschaft

Die vorliegende Habilitationsschrift hat sechs publizierte Originalarbeiten zur Grundlage. Drei der Arbeiten habe ich als alleiniger Erstautor und drei Arbeiten als alleiniger Letztautor veröffentlicht. Eine Publikation habe ich mit Frau Zainab Alwash in geteilter Erstautorenschaft veröffentlicht. Frau Alwash war Masterstudentin des Studiengangs „International Health“ der Berliner Charité und hat durch ihr außerordentliches Engagement in der qualitativ-wissenschaftlichen Begleitung des Aufbaus des Cancer Care Centre am KCMC einen vergleichbar großen Anteil an dieser Arbeit geleistet. Eine Überlappung mit einer anderen Habilitationsschrift ist dadurch nicht gegeben.

Die von der Fakultät geforderte Mindestanzahl von vier Erst- oder Letztautorenschaften wird auch ohne diese geteilte Erstautorenschaft erfüllt.

7. Bibliographie

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