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DISSERTATION

Untersuchungen zu Risikofaktoren für die Präsenz und Intensität der Tungiasis (Sandflohkrankheit) sowie zur krankheitsbezogenen Beeinträchtigung der Lebensqualität von Kindern in Kilifi County, Kenia

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Inhaltsverzeichnis

1 Zusammenfassung

Hintergrund: Die Tungiasis (Sandflohkrankheit) ist eine vernachlässigte Tropenkrankheit (*Neglected Tropical Disease*, NTD), die in großen Teilen der tropischen Welt verbreitet ist und mit gravierenden Komplikationen einhergehen kann. Sie wird durch die Penetration des weiblichen Sandflohs (*Tunga penetrans*) in die Haut hervorgerufen, welche eine starke Entzündungsreaktion im umliegenden Gewebe induziert und mit Juckreiz, erheblichen Schmerzen und Funktionseinschränkungen verbunden ist. Extraktionsversuche mit unsterilen Instrumenten führen zu einer bakteriellen Superinfektion oder einer Transmission von Viren wie HBV und HCV. Die epidemiologische Datenlage für den afrikanischen Kontinent ist äußerst spärlich.

Methoden: In einer prospektiven Studie wurde der Zusammenhang zwischen dem Schweregrad der akuten bzw. chronischen Tungiasis und der Lebensqualität von Kindern und Jugendlichen untersucht. In zwei Querschnittsstudien auf Haushalts- und Schulebene wurden Prävalenz, Intensität und potenzielle Risikofaktoren für das Auftreten der Erkrankung bzw. schwerer Infektionen analysiert.

Ergebnisse: Die Tungiasis beeinträchtigt das physische, psychische und soziale Wohlbefinden von Kindern und Jugendlichen im ländlichen Kenia erheblich. Eine Reduzierung der klinischen Pathologie unter effektiver Behandlung führte zu einer Rekonstitution der Lebensqualität. Die Prävalenz lag bei 25 % in der Allgemeinbevölkerung und bei 48 % in der untersuchten Schülerpopulation. Armutsassoziierte hygienische und architektonische Merkmale der Wohnumgebung wurden als Risikofaktoren identifiziert; eine mindere Qualität von Schul-Fußböden amplifizierte das Erkrankungsrisiko.

Konklusion: Möglichkeiten der Therapie und Prävention der Tungiasis sind vorhanden und müssen der ländlichen Bevölkerung mit hoher Priorität zugänglich gemacht werden. Die Befestigung von Wänden und Fußböden und eine Erweiterung der sogenannten WASH-Initiative (*Water, Sanitation and Hygiene*) sollten im Fokus der öffentlichen Gesundheitsversorgung stehen.

Abstract

Background: Tungiasis is a neglected tropical disease (NTD) which is widely spread in large parts of the tropical world and may be accompanied by severe complications. It is caused by the penetration of the female sand flea (*Tunga penetrans*) into the skin, which induces a strong inflammatory response in the surrounding tissue and is associated with itching, considerable pain and functional impairment. Attempts to remove the flea with non-sterile instruments lead to bacterial superinfection or transmission of viruses, e.g. hepatitis B and C. Epidemiological data for the African continent are still extremely scarce.

Methods: A prospective study was performed to investigate the relationship between the severity of acute or chronic tungiasis and the quality of life of children and adolescents. In two community- and school-based cross-sectional studies, prevalence, intensity and potential risk factors for the occurrence of tungiasis and severe disease were analyzed.

Results: Tungiasis substantially affects the physical, mental and social well-being of children and adolescents in rural Kenya. Under effective treatment, the reduction of clinical pathology correlated with the reconstitution of the quality of life. The prevalence was 25 % in the general population and 48 % in the examined student population. Poverty-related hygienic and architectural characteristics of the living environment were identified as risk factors; low-quality school floors amplified the risk of disease.

Conclusions: Therapy and prevention options do exist and must be made accessible to rural communities with high priority. The fastening of walls and floors as well as the extension of the so-called WASH initiative (*Water, Sanitation and Hygiene*) should be a main focus of public health care.

2 <u>Einleitung und Zielsetzung</u>

Die Tungiasis (Sandflohkrankheit) ist eine tropische Parasitose, welche durch in die Epidermis penetrierende Sandflohweibchen *(Tunga spp.)* hervorgerufen wird und Menschen wie Tiere betrifft [1]. Sie gehört zur Familie der vernachlässigten Tropenkrankheiten (*Neglected Tropical Disease*, NTD) [2] und ist in Südamerika, der Karibik und Afrika südlich der Sahara weit verbreitet. Menschen, die in großer Armut – in den Elendsvierteln der Großstädte oder im Hinterland – leben [3–10] sowie Kinder und ältere Menschen tragen die höchste Krankheitslast [6,7,11]. Nach Penetration in die Epidermis hypertrophiert der Floh und wächst innerhalb von zwei Wochen auf das 2000-fache seines initialen Volumens (sogenannte Neosomie) an [12]. Die Entwicklungsstadien in der Wirtshaut werden nach der Fortaleza-Klassifikation folgendermaßen unterteilt [12]: Stadium 1: Penetration (3 bis 7 Stunden); Stadium 2: beginnende Hypertrophie mit Ausscheidung von Fäzes (1 bis 2 Tage nach vollständiger Penetration); Stadium 3: maximale Hypertrophie auf 10 mm mit uhrglasähnlicher Wölbung und Expulsion von Eiern (3 Tage bis 3 Wochen nach Penetration); Stadium 4: Involutionsphase und Eliminierung der chitinösen Residuen (4 bis 6 Wochen nach Penetration); Stadium 5: Defektheilung mit typischer kreisrunder Aussparung im *Stratum corneum* (Monate bis Jahre nach Penetration). Die Stadien 1 bis 3 werden als vital, Stadien 4 und 5 als nicht-vital bezeichnet.

Der Druck des sich vergrößernden Flohkörpers auf das umliegende Gewebe, eine Fremdkörperreaktion sowie die nahezu konstante bakterielle Superinfektion der Läsion führen zu einer starken Entzündungsreaktion [13–16] mit Ödem-, Ulkus-, Abszess- und Fissurenbildung, die bei konstanter Reinfektion komplikativ bis zur Deformierung oder zum Verlust ganzer Zehen führen kann [13,14]. In Ermangelung von Alternativen werden die eingebetteten Parasiten mittels improvisierter, unsteriler Instrumente – Dornen, zugespitzte Hölzchen, Sicherheitsnadeln, Rasierklingen – manipuliert und mit wechselndem Erfolg extrahiert [14,17–19]. Die Benutzung desselben Instruments durch unterschiedliche Personen ist angesichts der hohen HIV-, HBV- und HCV-Prävalenz in der betroffenen Bevölkerung problematisch [19].

Die Tungiasis wird im öffentlichen Gesundheitswesen der Länder des globalen Südens weithin unterschätzt [2,11,20–22] und wurde bis vor Kurzem noch nicht einmal von der WHO als vernachlässigte Tropenkrankheit gelistet [23], was die Akquise von Fördermitteln zur Erforschung von Parasit und Umwelt sowie die Entwicklung von Therapien in hohem Maße erschwerte. Bisherige Interventionsbemühungen basieren im Wesentlichen auf Studienergebnissen aus Südamerika und Madagaskar [2,24,25], deren generelle Anwendbarkeit noch zu klären ist. In Ostafrika sind verlässliche Daten zur Verbreitung der Tungiasis so gut wie

inexistent, sodass die Planung von Kontrollprogrammen beeinträchtigt ist und einzelne Versuche, die Tungiasis zu beherrschen, bislang größtenteils durch Nichtregierungsorganisationen unternommen wurden [24].
Es ist anzunehmen, dass die durch die Tungiasis hervorgerufenen Beschwerden zu Einschränkungen der Leistungsfähigkeit und des Wohlbefindens führen. Dieser Aspekt wurde bislang jedoch nicht untersucht.
Die vom kenianischen Gesundheitsministerium empfohlene Therapie (Baden der Füße in 0,05 % $KMnO_4$) hat eine geringe Wirksamkeit [26] und fördert wegen der Blaufärbung der Haut eine Stigmatisierung. Neue hochwirksame Therapeutika sowie Präventivmaßnahmen auf der Basis pflanzlicher Repellentien stehen der Bevölkerung aus logistischen oder finanziellen Gründen nicht zur Verfügung [25–27]. Die Kenntnis von Risikofaktoren und die Umsetzung präventiver Maßnahmen stellen somit einen vielversprechenden Ansatz für die Infektionskontrolle dar.
Die Zielsetzungen meiner Dissertation waren:
1. den Einfluss der Tungiasis auf die Lebensqualität von Kindern systematisch zu erfassen.
2. grundlegende epidemiologische Daten zur Tungiasis in Kilifi County, Kenia zu erheben und Risikofaktoren im häuslichen sowie im schulischen Umfeld zu identifizieren.

3 Methodik

3.1 Studiengebiete und Studienpopulationen

Die drei Studien wurden in der Trockenzeit zwischen August und Oktober 2014, der Phase des Transmissionsmaximums, durchgeführt. Das Studiengebiet im Bezirk Kilifi im Osten Kenias teilt sich in zwei klimatisch unterschiedliche Zonen: Kakuyuni Sub-location im dicht bebauten Küstenstreifen mit tropischem Klima (Abb. 1A), und Malanga Sub-location, welche etwa 60 km landeinwärts von aridem Klima und dünnerer Besiedelung geprägt ist (Abb. 1B). Die Bewohner gehören zum Volk der Giriama, leben größtenteils von Köhlerei und Subsistenzlandwirtschaft und bauen Mais, Maniok, Mango und Kokosnuss an. Hofähnliche Strukturen von je zwei bis fünf Häusern sind über unbefestigte Wege durch angrenzendes Busch-, Acker- und Weideland miteinander verbunden. Die Ansiedlungen werden in der Regel von Großfamilien bewohnt, in denen gemeinsam gekocht und gewaschen wird, die Kinder erzogen werden und eventuell vorhandene sanitäre Anlagen ebenfalls gemeinsam genutzt werden. Katzen, Hunde und sonstige Haus- und Nutztiere streunen frei herum.

Abb. 1A und B: Hofstrukturen in Kakuyuni Sub-location und Malanga Sub-location.

Die stroh- oder wellblechgedeckten Häuser besitzen mehrheitlich Lehmwände und sandige Böden und bestehen selten aus mehr als zwei Räumen, in welchen durchschnittlich sechs bis acht Familienmitglieder dichtgedrängt zusammenleben. Patchwork-Konstellationen sowie alleinerziehende Mütter und Großmütter kommen häufig vor. Die Trink- und Nutzwasserversorgung ist unzureichend, nur wenige Häuser verfügen über improvisierte Latrinen. Abfälle werden verbrannt oder in der Umwelt verteilt. Analphabetismus, Arbeitslosigkeit und Alkoholismus verschärfen die prekäre ökonomische Situation dieser ländlichen Bevölkerung. Nur wenige Kinder besitzen Schuhe, ein Großteil muss den weiten Weg zur Schule barfuß bewältigen.

3.2 Studiendesign und Untersuchungsmethoden

3.2.1 Beeinträchtigung der Lebensqualität von Kindern mit Tungiasis

Die Lebensqualitätsstudie bestand aus einer Basisuntersuchung mit anschließender Therapie entsprechend den Empfehlungen des Gesundheitsministeriums sowie einer Folgeuntersuchung im Abstand von vier Wochen. Insgesamt wurden 50 an Tungiasis erkrankte Kinder in fünf Dörfern der Kakuyuni Sub-location identifiziert. Einschlusskriterien waren ein Alter von 5 bis 14 Jahren und das Vorhandensein von insgesamt mindestens sechs Sandflohläsionen an beiden Füßen, unabhängig vom Entwicklungsstadium und Manipulationsstatus.
Mithilfe eines Dorfgesundheitshelfers wurden Haushalte aufgesucht, in denen die Existenz von Patienten mit Tungiasis bekannt war, und das jeweils erste die Einschlusskriterien erfüllende identifizierte Kind in die Studie aufgenommen. Da die Tungiasis nahezu ausschließlich die Füße betrifft [11,17], wurde die körperliche Untersuchung auf diese Region beschränkt. Zu beiden Untersuchungszeitpunkten wurden Anzahl und Entwicklungsstadium der Tungiasisläsionen gemäß der Fortaleza-Klassifikation dokumentiert [12]. Zudem wurde die klinische Pathologie

semiquantitativ mittels modifizierter Indizes für akute (*severity score for acute tungiasis* = SSAT, 0 - 30 Punkte) und chronische Tungiasis (*severity score for chronic tungiasis* = SSCT, 0 - 32 Punkte) evaluiert (modifiziert nach [28]). Die Intensitäten von Spontanschmerz und Juckreiz wurden anhand von visuellen Analogskalen erfasst und gehen in den SSAT ein.

Zur Ermittlung der Beeinträchtigung der Lebensqualität diente der *Dermatology Life Quality Index* (DLQI) [29], welcher entsprechend der krankheitsspezifischen klinischen Pathologie sowie den kulturellen und sprachlichen Gewohnheiten kenianischer Kinder adaptiert wurde (nach [30,31]). Der abgeleitete *Tungiasis-assoziierte Dermatology Life Quality Index* (tr-DLQI) berücksichtigt sechs Kategorien von Lebensqualitätseinschränkungen (Schamgefühl, Mobilitätseinschränkung, Konzentrationsschwierigkeiten, Probleme in der Freizeitgestaltung, Beeinträchtigung von sozialen Kontakten, Schlafstörungen), deren Ausprägung verbal oder mittels visueller Analogskalen auf einen Punktwert zwischen 0 (nicht im Geringsten) und 3 (sehr stark) geschätzt werden soll. Der summierte Score kann zwischen 0 und 18 Punkten betragen, eine relevante Lebensqualitätseinschränkung besteht bei einem tr-DLQI ≥ 2 (nach [30]).

3.2.2 Haushaltsbezogene Risikofaktoren

Die Haushalts-Risikofaktorstudie wurde in drei Dörfern Kakuyunis und fünf Dörfern Malangas realisiert. Insgesamt wurden 1086 Individuen in 233 Haushalten in die Studie aufgenommen. Die Studiengebiete in Malanga und Kakuyuni wurden gewählt, da hier zuvor keinerlei Kontrolle der Tungiasis durchgeführt worden war. Dorfgesundheitshelfer leiteten die Tür-zu-Tür-Untersuchung an, da sie als Vertrauensperson und Dolmetscher den Kontakt für die Befragung erleichterten. In jeder Ansiedlung wurde nur ein Haushalt in die Untersuchung eingeschlossen, und jeweils die erste, bei Betreten des Geländes linker Hand befindliche, einzeln stehende Hütte aufgesucht und inspiziert. Zur Unterzeichnung der Einwilligungserklärung und Beantwortung der Interviewfragen musste mindestens eines der anwesenden Familienmitglieder volljährig (≥ 18 Jahre) sein.

Individuen jeden Alters und Geschlechts konnten in die Studie aufgenommen werden, solange sie innerhalb der vergangenen drei Monate mindestens vier Nächte pro Woche im ausgewählten Haushalt geschlafen hatten. Haushaltsmitglieder, die während des Besuchs nicht anwesend waren, wurden zu einem zweiten Zeitpunkt nachuntersucht. Hiernach noch nicht angetroffene Bewohner wurden eingeladen, sich innerhalb der nächsten Tage im lokalen Gesundheitszentrum vorzustellen, anderenfalls wurden diese Personen von der Studie ausgeschlossen. In einem strukturierten, vorab validierten Interview mit dem Haushaltsvorstand wurden demographische, sozioökonomische, umgebungs- und verhaltensassoziierte Informationen auf individueller bzw. Haushaltsebene erfragt. Da der Bargeldfluss den ökonomischen Status einkommensschwacher Bevölkerungsgruppen nicht adäquat widerspiegelt [32,33], verwendeten wir einen modifizierten Vermögenswertscore (nach [34]), der die folgenden Gegenstände erfasst und klassifiziert: Vorhandensein von Mobiltelefon, Gas-/Solarlampe (je 1 Punkt), Radio (2 Punkte), Fahrrad (3 Punkte), Fernsehapparat, Kühlschrank (je 5 Punkte) und Motorrad (10 Punkte). Der Score kann zwischen 0 und 27 Punkten liegen.

Die Füße und Hände der Studienteilnehmer wurden in einem standardisierten Verfahren auf das Vorhandensein von Sandflöhen untersucht [3] und der ektope Befall weiterer Körperregionen erfragt. Die Tungiasisläsionen wurden gemäß der Fortaleza-Klassifikation beurteilt [12]. Manipulierte Läsionen wurden ebenfalls dokumentiert und die Befallsintensität als leicht (1 bis 5 Läsionen), mittelgradig (6 bis 30) oder schwer (> 30) klassifiziert.

3.2.3 Schulbezogene Risikofaktoren

In der Schul-Risikofaktorstudie wurden 1829 Kinder an zwei Grundschulen in Kakuyuni (als KS1 und KS2 bezeichnet) und drei Grundschulen in Malanga (MS1, MS2 und MS3) untersucht. Die Schulen liegen mindestens 2 km voneinander entfernt und überschneiden sich in ihren Einzugsgebieten teilweise mit den in der Haushalts-Risikofaktorstudie untersuchten Dörfern. Die fünf Grundschulen wurden auf Empfehlung des örtlichen Gesundheitsamtes ausgewählt, da in diesen Tungiasis häufig sei. Das einzige Einschlusskriterium war, dass die untersuchten Kinder eingeschriebene Schüler der jeweiligen Schule waren. In einer Basisuntersuchung wurden die Füße aller 1829 Kinder und Jugendlichen klinisch standardisiert untersucht und vorhandene Sandflohläsionen erfasst. Das Vorgehen war identisch mit dem der Haushalts-Risikofaktorstudie. Um schulbezogene Risikofaktoren identifizieren zu können, wurden bauliche und strukturelle Charakteristika der Klassenräume (Zimmergröße, Schülerzahl, Beschaffenheit von Boden, Wänden und Dach) und der Schulgebäude dokumentiert.

Zur Detektion einer möglichen Veränderung der Befallsintensität bei fehlender Exposition gegenüber der Schulumgebung wurden 248 Schüler der Grundschule KS1 direkt nach Ende der vierwöchigen Augustferien ein zweites Mal untersucht.

Zudem wurde ein Teil der Schüler in strukturierten Interviews auf Giriama/Swahili zu infrastrukturellen, sozioökonomischen und Verhaltensfaktoren auf Haushaltsebene befragt und das Vorhandensein sowie der Zustand von Schuluniform und Schuhen beobachtend beurteilt.

In den Grundschulen KS1 und MS1 konnten alle Tungiasisfälle bei Kindern über 4 Jahren und ein jeweils direkt darauffolgender altersgleicher, gesunder Schüler als Kontrollperson in die

Erhebung eingeschlossen werden. Aus Zeitgründen wurde der Anteil an Interviews in den übrigen Schulen reduziert, indem nur die erste Hälfte der in willkürlicher Untersuchungsfolge identifizierten Fälle sowie deren chronologisch folgende Kontrollperson befragt wurden. Unvollständig beantwortete Interviews wurden nicht in die finale Analyse einbezogen, sodass von initial 923 (Teil-)Datensätzen lediglich 398 Fälle und 309 Kontrollen berücksichtigt werden konnten.

3.3 Datenanalyse

Unter Berücksichtigung einer erwarteten Abbruchquote von 5 % ergab die Stichprobenschätzung für die Lebensqualitätsstudie eine Mindestzahl von 45 Teilnehmern, um einen 25-prozentigen Unterschied in der Tungiasis-bezogenen Lebensqualitätseinschränkung vor und nach Therapie zu detektieren (Konfidenzniveau 95 %, Teststärke 80 %).

In der Planung der Haushalts-Risikofaktorstudie orientierten wir uns an Feldstudien aus Brasilien und Nigeria [35,36] und gingen von einem hypothetischen Verhältnis von Fällen zu Kontrollen von 1 zu 3, einer minimal nachweisbaren Odds Ratio von 1,75 sowie von 30 % Exponierten unter den Kontrollpersonen aus. Somit wurden 205 Fälle und 610 Kontrollen benötigt. Unter Berücksichtigung von Ungenauigkeit und Abbruchrate wurde daher die Untersuchung von 1000 Individuen angestrebt (Konfidenzniveau 95 %, Teststärke 90 %).

Die Berechnung der Stichprobengrößen für die Schul-Risikofaktorstudie basierte auf den folgenden Annahmen: Konfidenzniveau 95 %, Teststärke 80 %, 40 % Exponierte unter den Kontrollpersonen, minimal nachweisbare Odds Ratio 1,5. Aufgrund der altersbedingt höher zu erwartenden Prävalenz in der untersuchten Population wurde mit einem Fall-Kontroll-Verhältnis von 1 zu 1 kalkuliert, sodass mindestens 388 Fälle und 388 Kontrollpatienten benötigt wurden. In Anbetracht des sehr jungen Alters einiger Studienteilnehmer wurde mit 20 % unvollständigen Datensätzen gerechnet und die Zielzahlen entsprechend auf 930 Interviews erhöht.

Die Daten wurden in einer Excel-Datenbank (Excel Version 2013, Microsoft, Redmont, Washington, USA) gespeichert, auf Eingabefehler überprüft und mit dem Analysis ToolPack Add-In (Excel Version 2013, Microsoft, Redmont, Washington, USA) ausgewertet. Graphen wurden mithilfe des PowerPivot Add-Ins erstellt. Im Falle der Haushalts-Risikofaktorstudie wurden die Daten in SPSS (PASW Statistics 18.0, SPSS Inc., Chicago, IL, USA) übertragen, die Schul-Risikofaktoranalyse wurde in R (R Statistical Software, Version 2.14.2) durchgeführt. Da die Zielgrößen nicht normalverteilt waren, wurden die zentrale Tendenz und die Dispersion der Daten mittels Median und Interquartilsabstand (IQR) bestimmt. Zum Vergleich des modifizierten Dermatology Life Quality Indexes verschiedener Subgruppen sowie von Variablen vor und nach der Behandlung wurden der Mann-Whitney-U-Test und der Wilcoxon-Vorzeichen-Rang-Test für gepaarte Stichproben herangezogen. Korrelationen wurden anhand des Spearman-Rangkorrelationskoeffizienten, relative Häufigkeiten mit dem Chi-Quadrat- und dem Exakten Test nach Fisher berechnet.

In den Risikofaktorstudien wurde zunächst eine bivariate Analyse durchgeführt und Odds Ratios (OR) sowie 95 %-Konfidenzintervalle (95 % KI) berechnet. In einem zweiten Schritt wurden diejenigen Variablen, welche signifikant ($p < 0{,}05$) mit dem Auftreten von Tungiasis im Allgemeinen bzw. mit starker Infektion im Besonderen assoziiert waren, in ein multivariates logistisches Regressionsmodell mit schrittweisem Einschluss von Variablen eingegeben, um unabhängige Expositionsfaktoren zu identifizieren. Parameter, welche nur für volljährige Studienteilnehmer erhoben worden waren, wurden hierbei nicht berücksichtigt. Für Risikofaktoren, welche einer Intervention zugänglich erschienen, berechneten wir das Populationsattributable Risiko (*Population Attributable Fraction*, PAF).

Die innerhalb der Schulklassen als abhängig angenommenen Ergebniswerte der einzelnen Studienteilnehmer wurden mittels verallgemeinerter Schätzgleichungen ausgewertet. In der multivariaten Analyse von Faktoren, die potenziell mit dem Auftreten bestimmter Flohentwicklungsstadien nach den Schulferien verbunden waren, wurden Rate Ratios (RR) berechnet.

3.4 Ethische Aspekte

Die Studienteilnehmer bzw. deren Erziehungsberechtigte oder gesetzliche Vertreter wurden mündlich auf Englisch oder in einfach verständlichem Swahili/Giriama über Hintergrund, Ziele und Ablauf der Untersuchungen und Befragungen informiert. Fragen wurden ausführlich beantwortet, das Einverständnis zur Teilnahme schriftlich per Unterschrift oder Fingerabdruck dokumentiert und die Teilnehmer wurden auf das Recht, jederzeit ohne Angabe von Gründen ausscheiden zu können, hingewiesen. Die anschließende Untersuchung wurde zur Wahrung der Privatsphäre in einem separaten Raum und im Falle von Minderjährigen nur in Anwesenheit eines Erziehungsberechtigten oder -beauftragten durchgeführt. Den Studienteilnehmern wie auch allen sonstigen Bewohnern der Studiengebiete wurde eine kostenfreie, weiterführende Behandlung der Tungiasis durch einen Dorfgesundheitshelfer angeboten. Patienten mit komplizierter Tungiasis (bakterielle Superinfektion, ausgeprägte Ödeme) oder Nebenbefunden wurden zum nächstgelegenen Gesundheitsposten überwiesen. Die Studien wurden durch die Ethikkommission der Universität Kilifi genehmigt (Zulassungsnummer ERC/PhD/010/2014).

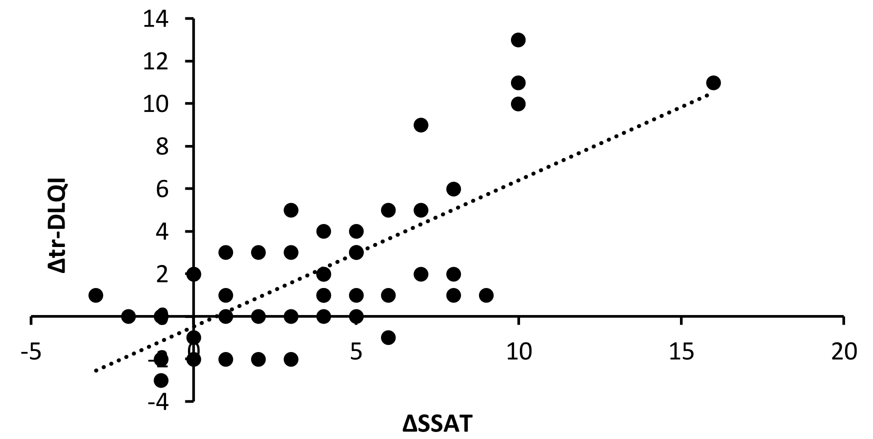
4 Ergebnisse

4.1 Beeinträchtigung der Lebensqualität von Kindern mit Tungiasis

50 Patienten konnten in die Studie zur hautbezogenen Lebensqualität eingeschlossen werden, 35 Jungen und 15 Mädchen. Der Altersmedian lag bei 8 Jahren, die Altersspanne zwischen 5 und 14 Jahren. Von den 3556 vorhandenen Läsionen waren 58 % manipuliert worden. Die Studienteilnehmer wiesen zum Zeitpunkt der Basisuntersuchung mindestens eine, im Median 33 manipulierte Läsionen auf. 54 % der Patienten hatten mehr als sechs vitale Sandflöhe. Der SSAT lag im Median bei 10, der SSCT bei 6 Punkten. Jungen waren hinsichtlich Befallsintensität (im Median 59 versus 43 Läsionen) und subsequenter klinischer Pathologie (SSAT 10 versus 8 Punkte) stärker betroffen als Mädchen.

96 % der Patienten gaben eine relevante Einschränkung der hautbezogenen Lebensqualität an (tr-DLQI ≥ 2), welche in 56 % der Fälle als moderat, in 22 % als schwer bis sehr schwerwiegend zu interpretieren war. Schlaf- und Konzentrationsstörungen wurden von den Betroffenen am häufigsten benannt (86 bzw. 84 %), soziale Ausgrenzung mit 62 % am seltensten. Keine der Kategorien wies einen signifikanten Unterschied zwischen den Geschlechtern auf. Die Lebensqualitätseinschränkung korrelierte stark mit der durch den SSAT gemessenen akuten Pathologie der Tungiasis ($\varrho = 0{,}74$, $p < 0{,}001$) sowie mit der Intensität von Schmerz ($\varrho = 0{,}82$, $p < 0{,}001$), Juckreiz ($\varrho = 0{,}61$, $p < 0{,}001$) und der Anzahl an vitalen Läsionen ($\varrho = 0.64$, $p < 0{,}001$). Der Schweregrad der chronischen Pathologie (SSCT, $\varrho = 0{,}27$, $p = 0{,}06$) sowie die Gesamtzahl aller Läsionen und der manipulierten Läsionen korrelierten nicht mit dem tr-DLQI ($\varrho = 0{,}23$, $p = 0{,}10$ und $\varrho = 0{,}004$, $p = 0{,}98$).

Grafik 1: Korrelation von individuellem Δtr-DLQI und ΔSSAT.



Δtr-DLQI: Differenz von tr-DLQI[Basisuntersuchung] und tr-DLQI[Nachuntersuchung]

ΔSSAT: Differenz von SSAT[Basisuntersuchung] und SSAT[Nachuntersuchung]

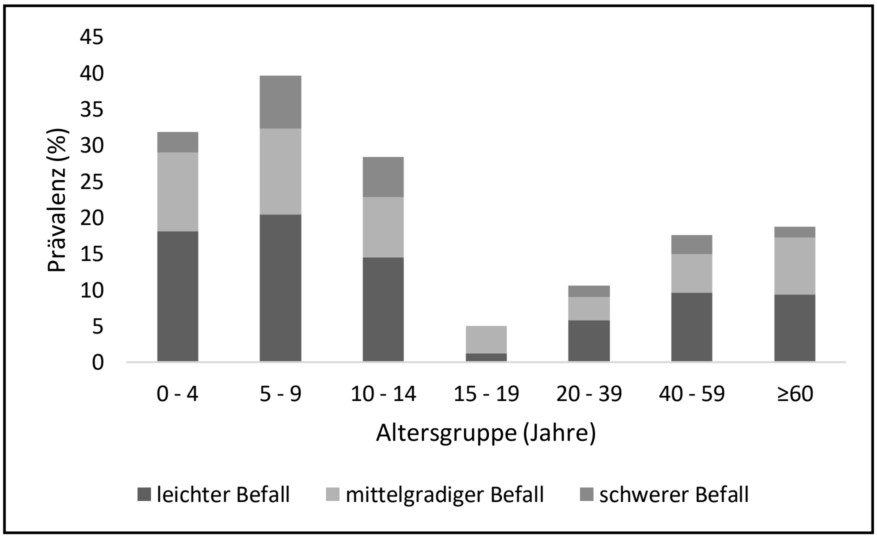
46 der 50 Patienten stellten sich nach einem Behandlungszeitraum von vier Wochen zur Nachuntersuchung vor. Der Schweregrad der akuten Pathologie fiel von initial im Median 10 Punkten (IQR 7,25 – 12) auf 7 Punkte (IQR 3,25 – 8) bei der

Nachuntersuchung (p < 0,001), begleitet von einer diskreten, jedoch signifikanten Verbesserung des tr-DLQI von 6 (IQR 4 – 8) auf 5 (1,25 – 6, p < 0,001) Punkte. Eine Linderung wurde vor allem in den Kategorien Konzentrationsschwierigkeiten (p = 0,001), Probleme in der Freizeitgestaltung (p < 0,001), Mobilitätseinschränkung (p = 0,003) und Schamgefühl (p = 0,007) wahrgenommen. Auf individueller Ebene fand sich eine hochsignifikant positive Korrelation zwischen der individuellen Abnahme des klinischen Schweregrades und der Besserung der dermatologischen Lebensqualität (ϱ = 0,61, p < 0.001, Grafik 1).

4.2 Haushaltsbezogene Risikofaktoren

Die Studienteilnehmer waren zwischen 4 Monaten und 80 Jahren alt, 58,6 % waren jünger als 15 Jahre. Durch eine Überrepräsentation der Altersgruppe zwischen 20 und 39 Jahren waren Frauen in unserer Studienpopulation signifikant stärker (57,3 %) vertreten als Männer (42,7 %). Ein Drittel der Erwachsenen waren Analphabeten, ein Drittel hatte eine Grundschule besucht und ein weiteres Drittel diese auch abgeschlossen. Sieben der 233 untersuchten Haushalte waren mit Strom versorgt, die große Mehrheit der Häuser hatte sandige Böden (89 %) und Lehmwände (84,5 %). In 84 % der Fälle musste Wasser von einem Gemeinschaftshahn in größerer Entfernung geholt werden. 88% der Haushalte besaßen Haustiere, am häufigsten Hühner und Ziegen.

Grafik 2: Altersspezifische Prävalenz und Intensität der Tungiasis.



Die Prävalenz der Tungiasis betrug 25 % in der allgemeinen Bevölkerung, 4 % waren an einer schweren Tungiasis (>30 Läsionen) erkrankt. In 42,5 % der Haushalte war mindestens ein Individuum von der Erkrankung betroffen. Die Befallsintensität war in etwa 50 % der Fälle leicht, in 35 % mittelgradig und in 15 % schwer. Die altersspezifische Prävalenz folgte einem S-förmigen Verlauf mit einem ersten Maximum in der Gruppe der 5- bis 14-jährigen Kinder, einem Rückgang der Häufigkeit bei Jugendlichen und Erwachsenen und einem erneuten Anstieg im Alter. Sie korrelierte positiv mit der altersspezifischen Häufigkeit

eines schweren Befalls (ϱ = 0,90, p = 0,0059), sodass sich unter 15- und über 40-Jährige nicht nur am häufigsten, sondern auch am schwersten infiziert präsentierten.
Die heterogene Verteilung der betroffenen Haushalte im Studiengebiet resultierte in einer hohen Variabilität der Tungiasis-Prävalenz unter den einzelnen Dörfern. Bahati und Yembe hatten die höchsten Prävalenzen (64,7 % bzw. 59,3 %, OR 21,80 und 17,29), während diese in Mtoroni lediglich 7,8 % betrug. Weitere signifikante Risikofaktoren aus der bivariaten Analyse waren Palmdächer (OR 4,36 für schwere Tungiasis) und Sand- (OR 4,31) bzw. Lehmböden (OR 2,23) im Wohnbereich, die Nutzung traditioneller Latrinen (OR 5,91) oder gänzlich fehlende sanitäre Anlagen (OR 6,19), ein niedriger Vermögenswertscore (OR 7,85 bei 0 bis 4 Punkten) und Analphabetismus (OR 3,37). Keine der untersuchten Tierspezies erwies sich in dieser Untersuchung als Risikofaktor für die Tungiasis beim Menschen.
In der multivariaten Analyse fand sich eine hohe Wahrscheinlichkeit für eine schwere Infektion bei Männern (OR 2,29) sowie bei Individuen, die sich nur einmal täglich wuschen (OR 2,23) oder ihr Wasser aus Pfützen schöpften (OR 25,48). Als Risikofaktoren für das Auftreten von Tungiasis im Allgemeinen wurden ein Alter unter 15 oder über 40 Jahren (OR 3,49 bis 12,88), das Waschen ohne Seife (OR 7,36), das Wohnen in einem Haus mit Lehmwänden (OR 3,35), eine hohe Personendichte im Schlafzimmer (OR 1,77) sowie direkt auf dem Fußboden schlafende Kinder (OR 1,68) identifiziert. Gemäß den kalkulierten PAF würden sich durch den Ersatz von Lehm als Bausubstanz 64,45 % der Fälle vermeiden lassen. Durch den Gebrauch von Seife sowie häufigeres Waschen könnten theoretisch 16,61 % bzw. 20,18 % der Erkrankungen verhindert werden.

4.3 Schulbezogene Risikofaktoren

Die untersuchte Schülerpopulation war zwischen 2 und 21 Jahren alt und umfasste 48 % Jungen sowie 52 % Mädchen. Alter und Geschlecht waren signifikant mit dem Auftreten von Läsionen assoziiert, wobei Kinder unter 15 Jahren (2- bis 9-Jährige: OR 1,57, 10- bis 14-Jährige: OR 1,35) bzw. Jungen (OR 2,37) das größte Erkrankungsrisiko hatten.
48 % der Schüler/-innen litten an Tungiasis, wobei 58 % von ihnen leicht, 31 % moderat und 11 % schwer betroffen waren. Die schulspezifischen Prävalenzen lagen zwischen 31 und 83 %. 86 % der Kinder wurden in Klassenräumen mit Wellblechdach, Betonwänden und rissigem, porösem (40 %) oder glattem (46 %) Betonboden unterrichtet, 14 % in Räumen mit Sand- bzw. Lehmboden, Lehmwänden und Palmdächern. Die Bodenbeschaffenheit erwies sich in der multivariaten Analyse als Confounder der schulspezifischen Prävalenz: lockere Fußböden aus Naturmaterialien zeigten sich als unabhängiger Risikofaktor und erhöhten die

Wahrscheinlichkeit zu erkranken um den Faktor 3. Sie traten jedoch lediglich in den Schulen MS2 und MS3 auf, in denen auch die höchsten Prävalenzen gefunden wurden. Das Vorhandensein von rissigem Betonfußboden stellte nur in der Schule MS2 einen signifikanten Risikofaktor dar (OR 11,54), in den übrigen 3 Schulen mit niedrigeren Prävalenzen und fehlender Koexistenz von sandigen Böden traten Tungiasisfälle bei glattem wie porösem Beton gleichermaßen auf. Klassenraumgröße und Schülerdichte spielten als Risikofaktoren keinerlei Rolle.
Die multivariate Analyse für die zu zwei Zeitpunkten untersuchte Population an KS1 bestätigte die in der Gesamtstudienpopulation gefundenen demographischen Risikofaktoren (männliches Geschlecht: OR 3,07, Alter < 10: OR 2,94) und identifizierte den Zeitpunkt der Untersuchung als unabhängige Variable. Die Prävalenz stieg von 31 % vor auf 44 % nach den Schulferien (OR 1,71) bei einem Anstieg der Gesamtzahl identifizierter Läsionen von 1402 auf 1705. Eine Analyse nach Entwicklungsstadien ergab, dass sich die Zahl vitaler Läsionen signifikant und unabhängig von Alter und Geschlecht von durchschnittlich 2,52 auf 0,80 nach den Ferien reduziert hatte (RR 0,30). Im Gegensatz dazu nahm die Zahl der manipulierten Läsionen signifikant zu und stieg bei Mädchen (von 3,06 auf 9,52 im arithmetischen Mittel) bzw. bei den 10- bis 14-Jährigen (von 3,94 auf 13,55) steiler an als bei Jungen bzw. bei Kindern anderer Altersstufen.
Die in der Befragung und durch die Beobachtung erfassten Merkmale waren – abgesehen vom Geschlecht – heterogen unter den Schulen verteilt, sodass diese in der multivariaten Analyse als Random Factor Berücksichtigung fanden. Der Zustand der Schuluniform war abhängig vom Geschlecht mit dem Auftreten von Tungiasis assoziiert: Jungen in zerschlissener Kleidung waren wahrscheinlicher (OR 4,30) infiziert als solche in gepflegter Uniform oder entsprechend gekleidete Mädchen. Ebenso war das Vorhandensein von offenen oder geschlossenen Schuhen nicht per se ein Risikofaktor. Mangelndes Schuhwerk in Kombination mit einer zerschlissenen Uniform war jedoch ein starkes Indiz für die Präsenz der Tungiasis (OR 5,32). Als Risikofaktoren in der häuslichen Umgebung der Kinder wurden die folgenden Faktoren identifiziert: Sand- bzw. Lehmboden (OR 1,88 und 1,65), ein außerhalb der Ansiedlung gelegener Gemeinschaftswasserhahn oder -brunnen als Wasserquelle (OR 1,63) sowie der seltene oder fehlende Gebrauch von Seife (OR 1,62 und 6,33). Die Frequenz des Füßewaschens war nicht signifikant mit dem Auftreten der Tungiasis assoziiert, die Nichtbeantwortung der diesbezüglichen Frage hingegen schon (OR 6,01).
Als signifikante Risikofaktoren für eine schwere Tungiasis wurden ein Alter unter 15 Jahren (OR 1,4 und 1,8) sowie im häuslichen – nicht jedoch im schulischen – Umfeld ein sandiger Boden

bzw. Lehmboden (OR 3,10 und 2,05), ein fehlender Zugang zu einem Wasserhahn oder Brunnen (OR 6,03) und seltenes Waschen der Füße nachgewiesen (OR 4,19). Zudem erwies sich das Halten von Hühnern als protektiver Faktor (OR 0,34). Die PAF sind in Tabelle 1 dargestellt.

Tabelle 1: Populationsattributables Risiko.

	Alle Infektionen				Schwere Infektionen (>30 Läsionen)			
Variable	**OR**	**AR**	**% Exponierte unter den Fällen**	**PAF %**	**OR**	**AR**	**% Exponierte unter den Fällen**	**PAF %**
Sandiger Boden im Klassenzimmer	2,99	0,67	21,5	14,3				
Sandiger Boden zu Hause	1,88	0,47	65,6	30,7	3,1	0,68	80,3	54,4
Lehmboden zu Hause					2,05	0,51	16,9	8,7
Fehlende Verwendung von Seife	6,3	0,84	6,1	5,1				
Seltene Verwendung von Seife	1,6	0,38	57,2	21,5				
Anderweitige Wasserquelle					6,03	0,83	4,2	3,5
Waschen seltener als 1 x tgl.					4,19	0,76	5,6	4,3
Keine Hühner					5,19	0,81	9,9	8,0

OR: Odds Ratio, AR: Attributables Risiko, PAF: Population Attributable Fraction

5 Diskussion

5.1 Beeinträchtigung der Lebensqualität von Kindern mit Tungiasis

Zum ersten Mal konnte gezeigt werden, dass die Tungiasis – in klassischen Tropenmedizinlehrbüchern mehr als Lappalie denn als Leiden abgehandelt – die Lebensqualität von Kindern signifikant mindert. Erkrankungen der Haut, ob immunologischer, toxischer, infektiöser oder parasitärer Genese, stellen für den Betroffenen nicht nur auf physischer, sondern ebenso auf mentaler und sozialer Ebene eine Belastung dar. Dies gilt insbesondere für Hautveränderungen an Körperstellen, die aufgrund ihres Ausmaßes, klimatischer Bedingungen oder gesellschaftlicher Konventionen in der Regel unbedeckt bleiben, Außenstehenden einen potenziell infektiösen Zustand oder mangelnde Hygiene suggerieren und somit zu Stigmatisierung und sozialer Ausgrenzung führen [30,37,38]. Besonders eindrücklich ist dies für das Krankheitsbild der lymphatischen Filariose, die zu extensiven Lymphödemen der Extremitäten und des Genitales führt [39,40], und für die Lepra [41].

Die in dieser Studie untersuchten Kinder wiesen ein breites Spektrum an klinischer Pathologie auf. Die Tatsache, dass bei der Basisuntersuchung alle Patienten manipulierte Läsionen trugen, zeugt von dem hohen Leidensdruck, dessen sich die Betroffenen in verzweifelten, amateurhaften Operationsversuchen zu entledigen versuchen. 96 % konstatierten eine relevante Einschränkung ihrer Lebensqualität – eine Frequenz, die durchaus mit Ergebnissen aus Untersuchungen anderer vernachlässigter Tropenkrankheiten wie Skabies, kutane Leishmaniose und kutane Larva migrans vergleichbar ist [30,42,43]. Patienten jener Studien schätzten den Grad ihrer Lebensqualitätseinschränkung jedoch weniger häufig als schwerwiegend ein.

Alle erfragten Beschwerden und Einschränkungen traten mit Frequenzen zwischen 62 und 86 % häufig auf, angeführt von Schlafstörungen. Es erscheint plausibel, dass Beschwerden wie Juckreiz und Schmerz in Ruhe stärker wahrgenommen werden und Ein- bzw. Durchschlafstörungen zur Folge haben können. Ein Mangel an ausreichendem und erholsamem Schlaf führt zu Erschöpfung, Dysthymie und Konzentrationsschwierigkeiten [44], der am zweithäufigsten benannten Einschränkung. Langfristig können Schlafstörungen zur Entwicklung von psychischen Problemen wie Angststörungen beitragen [44].

Die mit der Entzündungsreaktion verbundenen Schmerzen führen dazu, dass die Erkrankten beim Laufen nicht mit der gesamten Fußsohle auftreten und eine Art Watschelgang entwickeln, der sie bereits aus großer Entfernung als Tungiasispatienten entlarvt [45]. Die so verminderte Mobilität schränkt die Teilhabe an typischen Freizeitaktivitäten ein.

Die Tungiasis gilt selbst in armen, ländlichen Gegenden noch als Erkrankung der Ärmsten, die Kinder werden auf dem Schulhof verspottet, was bei den Betroffenen ein Gefühl von Scham auslöst und zu sozialer Ausgrenzung führt. Wie auch Schuster et al. in einer Studie zu Hakenwurm-assoziierter kutaner Larva migrans fanden wir keinen signifikanten Unterschied zwischen Jungen und Mädchen in Einschränkungsart und -häufigkeit [30].

Die positive Korrelation von Schweregradindex und dermatologischem Lebensqualitätsindex wie auch deren hochsignifikante Normalisierung unter Therapie legen die Annahme einer Ursache-Wirkungs-Beziehung zwischen Tungiasis und Lebensqualitätseinschränkung nahe. Dies wird unterstützt durch die Beobachtung, dass der tr-DLQI bei im Untersuchungszeitraum reinfizierten Patienten und unveränderter klinischer Pathologie keine Besserung zeigte, und unterstreicht den gesundheitsrelevanten Stellenwert der Tungiasis auf individueller wie auf Public Health Ebene.

5.2 Haushaltsbezogene Risikofaktoren

Die in unserem Studiengebiet erhobene Prävalenz von 25 % ist mit den Ergebnissen einer Erhebung in Zentral-Uganda vergleichbar, liegt jedoch deutlich unter den beobachteten Werten in ländlichen und urbanen Gebieten Brasiliens und Nigerias, in denen Prävalenzen bis 45 % auftraten [6,7,20,46,47]. Der S-förmige Kurvenverlauf der altersspezifischen Prävalenz stellt ein epidemiologisches Charakteristikum der Tungiasis dar, welches unabhängig von der geografischen Lage und der Gesamtprävalenz auftritt [6,7,11,35]. Dies wird möglicherweise durch alterstypische Verhaltensweisen und Exposition [6], eine zunehmende Dicke der schützenden Hornschicht [4,48], Geschicklichkeit bei der Extraktion [7] oder sorgfältigere Körperpflege erklärt. Mit dem Nachweis einer positiven Korrelation von Befallsintensität und Prävalenz – sowohl altersspezifisch als auch die gesamte Studienpopulation betrachtend [7,20,35,46,47] – untermauert diese Studie die Ergebnisse früherer Untersuchungen [6,11,49].

Bei der Tungiasis handelt es sich um eine Zoonose mit sylvatischem, peridomiziliärem und domestischem Zyklus [2], in welchem verschiedene Tierspezies – in Nordostbrasilien, Nigeria und Uganda vor allem streunende Katzen, Hunde und Schweine - als Reservoir fungieren können [35,47,50,51]. Obwohl in 88 % der untersuchten Haushalte Tiere lebten, konnte keine Spezies als Risikofaktor für das Auftreten der Sandflohkrankheit identifiziert werden. Wenngleich lediglich das Vorhandensein der Tiere auf dem Gelände ohne zusätzliche veterinärmedizinische Untersuchung dokumentiert wurde, unterstützt dies die Annahme eines gänzlich humanen, intradomiziliären Transmissionszyklus im Studiengebiet. Einen weiteren Hinweis hierauf liefert die Beobachtung, dass eine große Zahl an Personen pro Schlafzimmer und auf dem nackten Boden schlafende Kinder mit dem Auftreten der Tungiasis assoziiert waren. Es ist vorstellbar, dass nachts ausgestoßene und auf den Boden gefallene Eier sich in Rissen im Lehmboden sammeln, wenn dieser mit einem Reisigbesen gekehrt wird, in denen sie sich über ein Larven- und Puppenstadium zum adulten Floh entwickeln können [52,53]. Die typische Konstruktionsweise der Häuser mit Lehmwänden und Palmdächern bietet diesen Off-host-Stadien ein ideales Milieu, in welchem sie durch herabfallenden Sand und Staub vor Austrocknung geschützt sind [53].
Weitere signifikante Risikofaktoren der multivariaten Analyse waren mit einer eingeschränkten Körperhygiene assoziiert und sind mit früheren Erkenntnissen über das Reproduktionsverhalten von Sandflöhen vereinbar [12,54,55]. Demnach scheidet das bereits in der Epidermis befindliche Weibchen klebrige Fäzesfäden aus, welche sich in den dermalen Papillen um die Läsion festsetzen und deren Geruch männliche Sandflöhe zur Paarung anlockt. Wären Wasser und Seife zur regelmäßigen Reinigung der betroffenen Körperregionen verfügbar, würden dementsprechend vermutlich weniger Weibchen befruchtet und die Befallsrate – insbesondere unter Annahme einer größtenteils intradomiziliären Transmission – würde sinken.
Die bereits in Vorstudien [2,6] beschriebene heterogene Verteilung der Tungiasis in Endemiegebieten – in den fünf untersuchten Dörfern Malangas bspw. mit Prävalenzen zwischen

7,8 und 64,7 % innerhalb eines Radius von 2 km – konnte in dieser Studie nicht ursächlich aufgeklärt werden und bleibt Gegenstand einer detaillierten spatialen Analyse.
Wohn- und hygieneassoziierte Umstände waren am bedeutendsten mit dem Auftreten der Tungiasis und einem schweren Befall verbunden. Entsprechend den berechneten PAF könnten simple Maßnahmen zu einer flächendeckenden Kontrolle der Erkrankung beitragen, beispielsweise die Befestigung von Wänden und eine verbesserte Wasserversorgung. Aufgrund der desolaten finanziellen Situation der Landbevölkerung sind diese Maßnahmen jedoch ohne Hilfe von außen kaum von der Theorie in die Praxis umzusetzen. In einer Gesellschaft, in der ein Stück Seife als Luxusgut zu betrachten ist, liegt die Anschaffung höherwertiger Baumaterialien in weiter Ferne. Wie auch in anderen Teilen der Welt trifft die Tungiasis im ländlichen Kenia die Ärmsten der Armen am härtesten.

5.3 Schulbezogene Risikofaktoren

Auch in der zweiten Risikofaktorstudie zeigte die Tungiasis – sowohl innerhalb als auch zwischen den Schulen – eine unterschiedliche Prävalenz und Intensität. Die Gesamtprävalenz lag mit 48 % etwa doppelt so hoch wie in der Haushaltsstudie, was aufgrund der altersspezifischen Vulnerabilität der Studienpopulation gegenüber Sandflöhen plausibel ist. Das hohe Erkrankungsrisiko von unter 15-Jährigen und Jungen bestätigt die in anderen Teilen der Welt identifizierten demographischen Risikofaktoren [6,11,56–58].
Die Ergebnisse der Interviews sowie des Follow-ups nach den Schulferien indizieren, dass das höchste Erkrankungsrisiko mit sozioökonomischen Faktoren der Wohnumgebung der Schüler assoziiert ist. Ein unbefestigter Boden im Klassenraum stellte zwar einen unabhängigen Risikofaktor dar, kam jedoch nur in zwei Schulen vor, in deren Einzugsgebiet auch ein Großteil der Fußböden der Häuser aus Sand oder Lehm bestand. Durch eine Befestigung derselben könnte auf Haushaltsebene eine Reduktion der Tungiasisfälle um ein Drittel bzw. der schweren Fälle um die Hälfte erzielt werden; auf Schulebene könnte ein Siebtel der Erkrankungen verhindert werden.
Die Kombination aus fehlendem Schuhwerk [59] und einer zerschlissener Schuluniform wurde – insbesondere bei Jungen – als Prädiktor der Tungiasis identifiziert und kann als Indiz für schwere Armut gewertet werden. Wie auch in der haushaltsbasierten Untersuchung wurden die Verfügbarkeit von Wasser und der Gebrauch von Seife als sozioökonomisch determinierte Risikofaktoren bestätigt. Das höhere Erkrankungs- und Befallsrisiko von Jungen zwischen 10 und 14 Jahren spiegelt deren vergleichsweise geringes Wissen über Hygienepraktiken [60] und nachlässige Waschgewohnheiten [61] gegenüber Mädchen wider. Dies unterstreicht die

Wichtigkeit von Präventionsprogrammen für diese Zielgruppe, aber auch für deren Eltern: in einer indischen Studie wuschen sich 88 % aller Mütter selbst mit Seife, nutzten diese jedoch nur zu 21 % für ihre Kinder [62]. Die häufige Nichtbeantwortung der Frage nach den Waschgewohnheiten steht – als Ausdruck des mit der Erkrankung assoziierten Schamgefühls und der durch die Tungiasis perpetuierten Armut gewertet – im Einklang mit den Ergebnissen der Lebensqualitätsstudie.

Der nach den Schulferien beobachtete starke Anstieg manipulierter Läsionen – als Indikator von Extraktionsversuchen mit inadäquaten Instrumenten – und die daraus resultierende Prävalenzzunahme implizieren eine große Zahl an stattgehabten Infektionen während der Ferienzeit, mithin im häuslichen Umfeld. Die Interaktion zwischen dem Geschlecht und der Manipulation von neu aufgetretenen Sandflöhen ist ein weiterer Hinweis auf das Körperpflegeverhalten von Jungen.

Auch in der Schul-Risikofaktorstudie war keine Tierspezies signifikant mit dem Auftreten von Tungiasis assoziiert. Vielmehr war das Vorhandensein von Hühnern im Haushalt ein protektiver Faktor gegenüber einem schweren Befall, wobei es sich um einen weiteren Indikator des ökonomischen Status handeln könnte. Vorstellbar ist zudem, dass Hühner adulte Sandflöhe aufpicken [63,64] und die nicht pigmentierten Larven und immobilen Puppen aus tieferen Bodenschichten scharren, sodass diese infolge des veränderten Temperatur- und Feuchtigkeitsmilieus und der UV-Exposition zugrunde gehen [53].

Die Ergebnisse der haushaltsbezogenen Befragung von Schülern und der zuvor beschriebenen Haushalts-Risikofaktorstudie haben eine nahezu deckungsgleiche Schnittmenge, sodass schulbasierte Erhebungen ein zuverlässiges Instrument in der Tungiasis-Grundlagenforschung darstellen. Die gezielte Untersuchung der Füße bei guten Tageslichtverhältnissen und die Therapie von Hochrisikogruppen sind gegenüber haushaltsbasierten Interventionen zeit- und kosteneffektiv und können dazu beitragen, dass die wenigen vorhandenen finanziellen Mittel zur epidemiologischen Datenerhebung und Transmissionskontrolle flächendeckend eingesetzt werden [3]. Schwerstbetroffene Kinder, die aufgrund ihrer Mobilitätseinschränkung dem Unterricht fernbleiben, sowie behinderte und sehr alte Menschen würden einer solchen Maßnahme allerdings entgehen.

Insgesamt könnten über 70 % aller Tungiasisfälle durch technisch einfache Präventionsmaßnahmen, wie das Zementieren von Fußböden in Haushalten und Klassenräumen oder die Ausstattung mit robusten Kunststofffolien sowie das tägliche Waschen der Füße mit Seife, vermieden werden. Im Sinne des sechsten Ziels für nachhaltige Entwicklung der Vereinten Nationen sollte das tägliche Waschen der Füße mit Seife Eingang in das WASH-Konzept finden und in Schulen propagiert werden [65]. Die durchschnittlichen Kosten für die Befestigung eines typischen kenianischen Wohnhauses belaufen sich auf etwa 200 Dollar und sind für die betroffene Landbevölkerung kaum zu decken. Die Erforschung lokal umsetzbarer Alternativen zur Bodenversiegelung sowie die Befestigung von Klassenzimmerböden muss von den zuständigen Behörden mit Priorität vorangetrieben und finanziell unterstützt werden.

5.4 Schlussfolgerungen

1. Mittels eines einfachen diagnostischen Instruments konnte gezeigt werden, dass eine Ursache-Wirkungs-Beziehung zwischen der vernachlässigten Tropenkrankheit Tungiasis und einer Einschränkung der Lebensqualität von Kindern im ärmlichen Milieu des ländlichen Kenias besteht. Die Bereitstellung existierender effektiver und sicherer Therapeutika und präventiver Maßnahmen sowie die Entwicklung und Zulassung erschwinglicher Mittel muss vorangetrieben werden, um die durch die Tungiasis verursachte Krankheitslast zu vermindern.
2. Die Tungiasis tritt in der ländlichen Region Kilifis mit hoher Prävalenz und Krankheitslast auf. Armutsassoziierte Faktoren, wie eine insuffiziente Wasserversorgung oder bauliche Mängel, konnten als Risikofaktoren identifiziert werden und bieten einen Ansatzpunkt für Maßnahmen der Infektionsprävention auf Haushaltsebene.
3. Zwar spielen im Studiengebiet schulassoziierte Faktoren für das Infektionsrisiko eine geringfügigere Rolle als die häusliche Umgebung, doch können eine Befestigung von Klassenzimmerböden sowie eine Ergänzung der WASH-Kampagne um eine Fußhygiene-Empfehlung das Transmissionsrisiko senken. Schulbasierte epidemiologische Untersuchungen stellen eine simple, kostengünstige und verlässliche Alternative zu haushaltsbasierten Studien dar.

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Eidesstattliche Versicherung

„Ich, Susanne Wiese, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „Untersuchungen zu Risikofaktoren für die Präsenz und Intensität der Tungiasis (Sandflohkrankheit) sowie zur krankheitsbezogenen Beeinträchtigung der Lebensqualität von Kindern in Kilifi County, Kenia“ selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe. Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung (siehe „Uniform Requirements for Manuscripts (URM)“ des ICMJE -*www.**icmje**.org*) kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) entsprechen den URM (s.o) und werden von mir verantwortet.
Meine Anteile an den ausgewählten Publikationen entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Betreuer/in, angegeben sind. Sämtliche Publikationen, die aus dieser Dissertation hervorgegangen sind und bei denen ich Autor bin, entsprechen den URM (s.o) und werden von mir verantwortet.
Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

Datum | Unterschrift

<u>Anteilserklärung</u>

Susanne Wiese hatte folgenden Anteil an den folgenden Publikationen:

Publikation 1: Wiese S, Elson L, Feldmeier H. Tungiasis-related life quality impairment in children living in rural Kenya. PloS Neglected Tropical Diseases. 2018;12(1):e0005939. doi:10.1371/journal.pntd.0005939.
<u>Beitrag im Einzelnen:</u> Beteiligung an der Planung der Studie, Durchführung der Studie in Kenia, Erhebung der klinischen Daten, Fotodokumentation, Dateneingabe und -analyse, Erstellen aller Grafiken und Tabellen, Verfassen des Textes

Publikation 2: Wiese S, Elson L, Reichert F, Mambo B, Feldmeier H. Prevalence, intensity and risk factors of tungiasis in Kilifi County, Kenya: I. Results from a community-based study. PLoS Neglected Tropical Diseases. 2017;11(10):e0005925. doi: 10.1371/journal.pntd.0005925.
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Druckexemplare der ausgewählten Publikationen

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Tungiasis-related life quality impairment in children living in rural Kenya

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Abstract

Background

Tungiasis (sand flea disease) is a neglected tropical skin disease caused by female sand fleas (*Tunga spp.*) embedded in the skin of the host. The disease is common in sub-Saharan Africa and predominantly affects children living in impoverished rural communities. In these settings tungiasis is associated with important morbidity. Whether tungiasis impairs life quality has never been studied.

Methods

The study was performed in 50 children with tungiasis, living in resource-poor communities in coastal Kenya. Based on the Dermatology Life Quality Index (DLQI) a tool was developed to determine life quality impairment associated with tungiasis in children, the tungiasis-related Dermatology of Life Quality Index (tungiasis-related-DLQI). Pain and itching were assessed using visual scales ranging from 0–3 points. The intensity of infection and the acute and chronic severity of tungiasis were determined using standard methods.

Results

Seventy eight percent of the patients reported a moderate to very large effect of tungiasis on life quality at the time of the diagnosis. The degree of impairment correlated with the number of viable sand fleas present in the skin (rho = 0.64, p < 0.001), the severity score of acute clinical pathology (rho = 0.74, p < 0.001), and the intensity of pain (rho = 0.82, p < 0.001). Disturbance of sleep and concentration difficulties were the most frequent restriction categories (86% and 84%, respectively). Four weeks after curative treatment, life quality had improved significantly. On the individual level the amelioration of life quality correlated closely with the regression of clinical pathology (rho = 0.61, p < 0.001).

Conclusion

The parasitic skin disease tungiasis considerably impairs life quality in children in rural Kenya. After effective treatment, life quality improves rapidly.

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Author summary

Although tungiasis (sand flea disease) is associated with important morbidity and affects millions of people in South America, the Caribbean and sub-Saharan Africa, it has been largely ignored by health care providers up to now. In this study we show that the restriction of life quality due to tungiasis goes far beyond physical aspects and that the disease is also a mental and emotional strain on affected children in rural Kenya. Almost eighty percent of the diseased individuals reported a moderate to very large effect of tungiasis on their life quality. The degree of perceived life quality impairment correlated with the number of embedded sand fleas and pain. Sleep disturbance and concentration difficulties were the most frequent impairment. Effective treatment led to a rapid improvement of pathology and, subsequently, to an improved quality of life. The results of this study give substantial evidence that tungiasis is an important health hazard deserving more attention from policy makers and international donors.

Introduction

Tungiasis (sand flea disease) is a parasitic skin disease caused by female sand fleas (*Tunga spp.)* penetrated into the skin of humans or animals [1]. It belongs to the ever-growing group of neglected tropical diseases (NTDs) which are infectious diseases prevalent in the tropical and subtropical regions and characterized by affecting the health of the world's poorest people and limiting their productivity. Tungiasis is particularly neglected in the sense that hitherto little research has been carried out with regard to disease burden and that health care providers in endemic areas commonly ignore the condition. Sand flea disease predominantly affects people living in poverty: in shanty towns at the periphery of metropolitan areas, in the rural hinterland or in isolated communities at the coast in South America, the Caribbean and sub-Saharan Africa including Madagascar [2–9]. Children and the elderly bear the highest disease burden [5,6,10]. In these population groups prevalence may be as high as 65%. Children frequently carry dozens of embedded sand fleas simultaneously [5,10].

In endemic areas 95 to 98% of all tungiasis lesions occur at the feet [10,11]. The toes, the sole and the heel are typical predilection sites [12]. Once embedded in the skin, the female sand flea undergoes a massive hypertrophy, and within two weeks reaches the size of a pea. Through an opening of about 250 μm the parasite remains in contact with the environment [13]. Being a continuously enlarging and biologically active foreign body located in the epidermis, embedded sand fleas cause an intense inflammatory response [12,14,15]. Bacterial superinfection is common and intensifies the inflammation [16]. Intense pain and itching are almost constant [13]. Frequent sequels are suppuration, ulcers, deep fissures, periungual oedema as well as deformation of nails and toes [12,14]. Although an effective and safe treatment exists it is not yet available in endemic countries [17–19]. Therefore, embedded sand fleas are removed by inappropriate sharp and non-sterile instruments such as needles, safety pins or razor blades [10,19]. This further increases the risk of bacterial superinfection and intense inflammation. Constant re-infection–as is the rule in endemic settings—impairs mobility, eventually leads to mutilation of the feet and immobilization of the patient. Anecdotal observations suggest that the restricted mobility may have a detrimental effect on household economics and impair school performance in children, mainly due to high absenteeism [19].

It is reasonable to assume that tungiasis causes mental strain and distress. In a setting where people rarely wear closed shoes the disease cannot be hidden in public and, since it is associated with poverty, it stigmatizes its victims [19]. In school, children are teased and ridiculed.

Whether tungiasis has an impact on life quality has never been investigated in a systematic manner. This study, therefore, aimed at assessing life quality in children living in a tungiasis-endemic area in rural Kenya.

Materials and methods

Study area and population

The study was performed in Kakuyuni Sublocation, Kilifi County, coastal Kenya, from September to October 2014. In the area, tungiasis is endemic with prevalences ranging from 30 to 85% in school-age children as determined in a school survey prior to the study (S1 Appendix).

Demographic data were collected within the larger survey addressing the epidemiology of tungiasis in the area. In Kilifi county communities are small and consist of two to five homesteads—clusters of houses—which are located about 100 m from each other, separated by fields or bushland. Usually four to six children sleep together with their parents in the same room, frequently on rugs put on the floor, more seldom on a dilapidated mattress, and rarely in a bed. Eighty five percent of the rooms do not have a solid floor, facilitating the propagation of the parasite inside the house. Eighty eight percent of the households have domestic animals such as goats, chicken, cats and dogs. In 89% of the homesteads the income is less than the official minimum wage of US$ 2 per day and thus fall in the lowest income bracket. School- age children very rarely own shoes and make their long way to school barefooted [20].

Study design

Community health workers were asked to identify households with tungiasis or to find out where they knew tungiasis had occurred previously. Children aged 5 to 14 years with at least six tungiasis lesions (viable, non-viable or manipulated) were eligible for the study.

A total of 50 patients–between 2 and 15 children in each case—were recruited from five villages. In order to avoid family-related inclusion bias only the first child in a household identified to have tungiasis was eligible for the study.

The intensity of infection (number of embedded sand fleas) and severity of tungiasis was determined by standardized procedures [5,21]. Since in endemic areas female sandfleas almost constantly penetrate the skin of the feet, the examination was limited to this topographic site [10,11].

Eligible patients were explained the procedure and a caregiver (usually the mother) was asked for informed written consent. The feet of the patient were carefully washed with soap in a bucket. Thereafter, the feet were thoroughly examined by the principal investigator (SW) in a room in which the privacy of the patient was guaranteed. Lesions were staged according to the Fortaleza classification and counted [13]:

- stage I: penetrating sand flea
- stage II: brownish/black dot with a diameter of 1–2 mm
- stage III: circular yellow-white watch glass-like patch with a diameter of 3–10 mm and with a central black dot
- stage IV: brownish-black crust with or without surrounding necrosis

Stage I to III are viable sand fleas; in stage IV the parasite is dying or already dead [12,21].

Lesions manipulated with a sharp instrument, such as a needle, a safety pin, a thorn or a razor blade were documented as manipulated lesions. Patients were not asked who had tried to remove embedded sand fleas.

Clinical pathology was assessed semi-quantitatively, using previously established severity scores for acute and chronic tungiasis (SSAT; SSCT) [21]. The SSAT varies from 0–30 points, the SSCT from 0–32 points. Pain and itching were assessed using visual scales ranging from 0–3 points (S2 Appendix). Deliberately, the figures were kept very simple to make them understandable even for small children with little school education.

Tungiasis-specific Dermatology Life Quality Index (DLQI)

The DLQI is a simple tool widely used to determine skin-associated life quality impairment. The English original was developed by Finlay and Khan [22], and is available at http://www.cardiff.ac.uk/dermatology/quality-of-life/. The DLQI is validated for an array of skin diseases of infectious and non-infectious origin [23,24].

In a first step, we modified the original questionnaire such that the tool measures the characteristic sequels of an inflammatory parasitic skin disease located at the feet. Next, we adapted the wording of the questions to the vocabulary and attitudes of Kenyan children. This resulted in a tungiasis-related DLQI with six categories of impairment and a score ranging from 0 to 18 points (S3 Appendix). Categories of impairment are as follows: feeling of shame, impairment of leisure activities, difficulty in walking, impairment of concentration during classes, social exclusion and sleep disturbances. The last four of these six categories were assessed using visual analogue scales (S2 Appendix), the first two just verbally.

The tungiasis-related DLQI was translated into Swahili, pre-tested in children, back-translated into English, then refined and translated into Swahili again. The questions were read out loudly and explained to the patients in a standardized manner by one of the native Swahili-speaking community health workers.

Children were shown the visual scales, depicting the categories of impairment one by one and were asked to point to the corresponding figure with their fingers. Answers were categorized as follows: no restriction perceived = 0, only a small restriction perceived = 1 point, important restriction perceived = 2 points, severe restriction perceived = 3 points. The points for each category were added up to form the tungiasis-related DLQI (Table 1).

Immediately after examination and interview the patients were referred to the local health centre for treatment. There they were treated according to national guidelines (http://www.jigger-ahadi.org/National Policy Guidelines for Prevention and Control.pdf; accessed November 29, 2016).

Patients were asked to present themselves at a determined location, usually the school, four weeks after treatment for follow up.

Statistical analysis

The data were entered into an Excel database (Excel Version 2013, Microsoft, Redmont, Washington, USA) and checked for errors which might have occurred during data entry. The data analysis was carried out using the Analysis ToolPack Add-In (Microsoft, Redmont,

Table 1. Interpretation of the tungiasis-related DLQI scores.

Scores	Assumed impact on patient's life quality
0–1	None
2–3	Small
4–8	Moderate
9–13	Large
14–18	Very large

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Washington, USA). The median and the interquartile range were calculated as indicators of central tendency and dispersion of the data, respectively. Since the data did not follow a normal distribution, non-parametric tests were used. The Mann-Whitney-U test was used to compare the modified Dermatology Life Quality Index (mDLQI) between subgroups of patients, and the Wilcoxon matched pairs signed rank test for the comparison of variables before and after treatment. The Spearman rank correlation coefficient was calculated to determine the significance of correlations. Relative frequencies were compared with the Chi-squared and Fisher exact tests.

The sample size estimate was based on the assumption of a 25% difference in tungiasis-related life quality impairment before and after treatment. Estimating a dropout rate of 5%, 45 patients were needed for complete data analysis (probability = 0.95; power of the test = 0.80).

Ethical considerations

The study was approved by the Ethics Review Committee at Pwani University, Kilifi County; approval number ERC/PhD/010/2014. The custodians and their protégés were informed about the objectives and procedures of the study in Swahili. The right to deny participation and withdraw consent at any given time was clearly explained.

The informed consent form was read out loud word by word in Swahili and explained further when required; questions of the custodian and the children were discussed and answered by a community health worker. Informed assent was obtained from the patients before examination and treatment. Written consent was obtained via fingerprint or signature from the legal guardian or the headmaster of the school in which the patient was enrolled. Participants were only examined in the presence of their mother or the headmaster.

For other illnesses requiring treatment a referral form was prepared by a community health worker, and patients were referred to the Health Facility in Kakuyuni. Treatment was also made available for household members with tungiasis who did not participate in the study.

Results

Fifty patients were included in the study, 35 of them male and 15 female. The demographic and clinical characteristics are summarized in Table 2. The median age was 8 years (range 5–14). Fifty four percent of the patients had more than six viable lesions (boys 57%, girls 47%). The maximum number of lesions was 457; 162 of them viable. Severity scores for acute and chronic tungiasis were: median SSAT 10 (maximum 27) and median SSCT 6 (maximum SSCT 11), respectively. Of the total 3,556 lesions present at baseline 58% had been manipulated by the patient or the caregiver. All participants showed at least one manipulated lesion, the median number being 33 (maximum 196). Overall, the intensity of tungiasis and the severity of disease was higher in boys than in girls.

The tungiasis-related DLQI showed that 78% of the patients reported a moderate to a very large restriction of their life quality (Table 3). The majority of the patients (56%, Fig 1) showed a moderate impairment corresponding to a median tungiasis-related DLQI of 6 points (25^{th} and 75^{th} percentile 4–8.5 for boys and 3.5–8 for girls, respectively). Sleep disturbance and concentration difficulties in class were the impairment categories most commonly reported (Table 4). None of the restriction categories differed between boys and girls.

There was a strong correlation between the severity of the acute clinical pathology as measured by the SSAT and the impairment of the life quality (rho = 0.74, $p < 0.001$, Fig 2). The intensity of pain (as assessed by the visual scale) showed an even stronger correlation with the tungiasis-related DLQI (rho = 0.82, $p < 0.001$). The intensity of itching was less strongly correlated (rho = 0.61, $p < 0.001$). There was only a weak correlation between tungiasis-associated

Table 2. Demographic and clinical characteristics of children with tungiasis (n = 50).

Characteristic		N (%)	
	total	Male	Female
Sex	50 (100)	35 (70)	15 (30)
Age (years)			
Median	8	9	8
Range	5–14	5–14	5–14
Clinical pathology		N (%)	
Erythema/warmness/oedema	43 (86)	29 (83)	14 (93)
Suppuration/ulcer/abscess	27 (54)	21 (60)	6 (40)
Local pain (points)*			
0	6 (12)	4 (11)	2 (13)
1	19 (38)	11 (31)	8 (53)
2	15 (30)	11 (31)	4 (27)
3	10 (20)	9 (26)	1 (7)
Itching (points)*			
0	3 (6)	2 (6)	1 (7)
1	32 (64)	22 (63)	10 (67)
2	9 (18)	6 (17)	3 (20)
3	6 (12)	5 (14)	1 (7)
Number of lesions	**Median (IQR)**		
All lesions types	52.5 (40–81.5)	59 (41.5–85.5)	43 (27–75)
Viable lesions	7 (3–12.75)	8 (4–15.5)	4 (1–7.5)
Non-viable lesions	12.5 (6–19.8)	13 (6.5–13)	9 (4.5–18.5)
Manipulated lesions	33 (25–48.75)	37 (26–50)	31 (14–48)
Severity scores	**Median (IQR)**		
SSAT	10 (7.25–12)	10 (8–14.5)	8 (7–10.5)
SSCT	6 (4–7.5)	6.5 (4–8)	6 (4.5–6)

* indicated by the patient using a visual scale; see Material and methods

IQR: interquartile range

SSAT: severity score for acute tungiasis

SSCT: severity score for chronic tungiasis

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chronic pathology as measured by the SSCT and the tungiasis-related DLQI (rho = 0.27, p = 0.06). Whereas the total number of lesions and the number of manipulated lesions did not correlate with the tungiasis-related DLQI (rho = 0.23, p = 0.10 and rho = 0.004, p = 0.98, respectively), the number of viable lesions did (rho = 0.64, $p < 0.001$).

Of the 50 patients, 46 presented again four weeks after treatment. In these patients acute clinical pathology had decreased significantly: median SSAT at baseline = 10 (interquartile range 7.25–12) versus 7 at follow up (interquartile range 3.25–8; $p<0.001$). This was accompanied by a slight though significant decrease of the tungiasis-related -DLQI: median = 6 (interquartile range 4–8) versus 5 (interquartile range 1.25–6; $p<0.001$, Table 5). The patients noted a clear amelioration in the restriction categories; concentration difficulty in class and impairment of leisure activities (p = 0.001 and $p < 0.001$, respectively) as well as feeling of shame and walking difficulties (p = 0.007 and p = 0.003). On the individual level there was a highly significant correlation between the reduction of acute clinical pathology and the amelioration of life quality (rho = 0.61, $p < 0.001$; Fig 3).

Table 3. Tungiasis-related life quality impairment (n = 50).

Tungiasis-related DLQI-scores	Impact on life quality	N (%) Total	N (%) male	N (%) female	P-value (♂ versus ♀)
(0–1 points)	No effect	2 (4)	1 (3)	1 (7)	0.51
(2–3 points)	Small effect	9 (18)	6 (17)	3 (20)	1.00
(4–8 points)	Moderate effect	28 (56)	19 (54)	9 (60)	0.76
(9–13 points)	Large effect	10 (20)	8 (23)	2 (13)	0.70
(14–18 points)	Very large effect	1 (2)	1 (3)	0 (0)	1.00

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Discussion

The group of 50 tungiasis patients enrolled in the study exhibited a broad spectrum of tungiasis-associated pathology, from moderate to severe disease. The fact that all children had manipulated lesions emphasizes that the embedded fleas were causing suffering, and in an act of despair, either they themselves or their caregivers tried to relieve that suffering by physical removal of the flea. In fact, 96% of the patients perceived their life quality to be impaired and 78% considered the impairment moderate to severe according to our mDLQI. This frequency of life quality impairment is similar to those reported from studies in patients with other neglected tropical parasitic skin diseases such as scabies, hookworm-related cutaneous larva migrans and cutaneous leishmaniasis [25–27]. However, patients with these other skin diseases classified the impairment as severe less frequently than patients with tungiasis.

Other than social exclusion, all impairment categories were reported in similar frequencies (range 62 to 86%) to each other. Sleep disturbances due to pain and itching were perceived as particularly impairing. This is plausible, because itching usually intensifies at night, and pain is perceived more intensive in a quiet environment when a person tries to fall asleep. A lack of sufficient and re-generative sleep leads to tiredness, bad mood and concentration difficulties in class, another impairment category noted by the patients. In the long term, sleep disorders might cause the development of psychological problems such as anxiety [28].

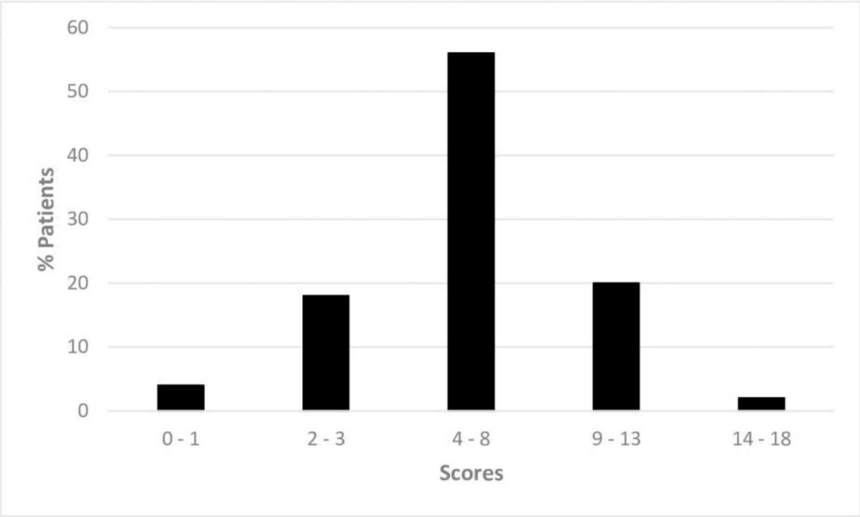

Fig 1. Distribution of the tungiasis-related DLQI scores (n = 50).

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Table 4. Restriction categories in patients with tungiasis (n = 50).

Restriction category	N (%) Total	N (%) male	N (%) female	P value (♂ versus ♀)
Sleep disturbances	43 (86)	32 (91)	11 (73)	0.18
Concentration difficulty	42 (84)	30 (86)	12 (80)	0.68
Feeling of shame	38 (76)	28 (80)	10 (67)	0.47
Restriction of leisure activities	38 (76)	28 (80)	10 (67)	0.47
Walking difficulty	37 (74)	26 (74)	11 (73)	1.00
Social exclusion	31 (62)	21 (60)	10 (67)	0.76
Tungiasis-related DLQI score				
Median (IQR)	6 (4–8)	6 (4–8.5)	6 (3.5–8)	0.41

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To alleviate the pain patients avoid placing the whole foot on the ground while walking leading to a classical gait which is readily recognized as a tungiasis patient from a long distance [29]. Obviously, impaired mobility limits the typical leisure activities of children in rural Africa.

Since children with tungiasis are ridiculed at school and because it is widely known that tungiasis affects the poorest of the poor, it is understandable that the feeling of shame and stigmatization are perceived as important restrictions. Probably, both restriction categories are also interlinked with social exclusion. Since the skin alterations are located on visible body parts, they are difficult to conceal and, on the long run, may lead to withdrawal and/or exclusion from society. Leprosy is paradigmatical for such sequels [30]. Patients may be confronted with ignorance or misconceptions regarding the aetiology of their skin disease, such as the fear that the condition is contagious or caused by poor personal hygiene–assumptions eventually leading to stigmatization [31,32]. This is the case, for instance, in lymphatic filariasis, a parasitic skin disease leading to gross lymphoedema of legs, arms and the genitals [33,34]. Stigmatization is detrimental to the well-being of the patient, causing distress and potentially inducing

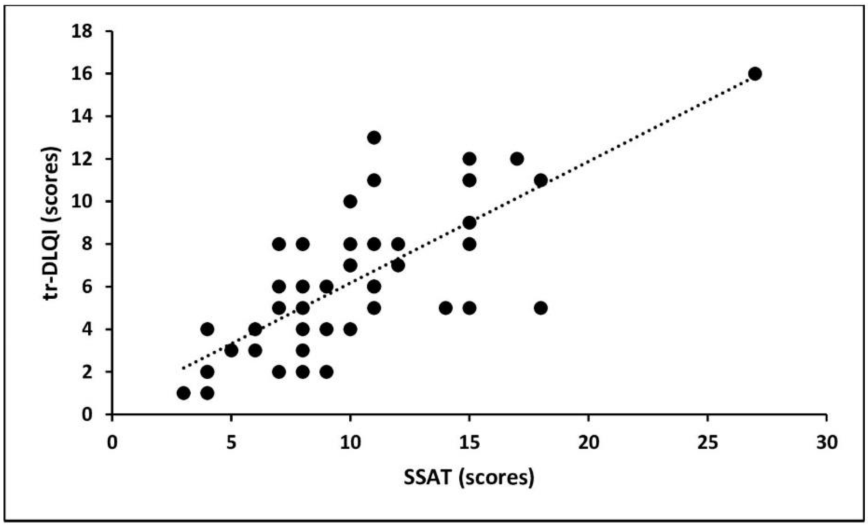

Fig 2. Correlation between severity of tungiasis measured by SSAT and the tungiasis-related DLQI (rho = 0.74, $p < 0.001$); dotted line = regression curve.

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Table 5. Improvement of clinical pathology and of life quality four weeks after treatment (n = 46).

Category of impairment	N (%) before treatment	N (%) after treatment	P value
Sleep disturbances	39 (85)	34 (74)	0.332
Concentration difficulty	39 (85)	25 (54)	0.001
Feeling of shame	34 (74)	25 (54)	0.007
Restriction of leisure activities	35 (76)	23 (50)	<0.001
Walking difficulty	34 (74)	25 (54)	0.003
Social exclusion	29 (63)	24 (52)	0.087
tr-DLQI scores			
Median (IQR)	6 (4–8)	5 (1.25–6)	<0.001
SSAT score			
Median (IQR)	10 (7.25–12)	7 (3.25–8)	<0.001

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mental disorder [32,35]. We did not find any significant difference in impairment quality and frequency between boys and girls. A similar observation was made by Schuster et al. in patients with hookworm-related cutaneous larva migrans living in a slum in Manaus, Brazil [25].

The importance of this study is multifold. For the first time, it was shown that tungiasis—a parasitic skin disease still considered to be a nuisance rather than an important parasitic disease in standard text books–impairs life quality. The impairment categories perceived by the patients do not only reflect the clinical pathology caused by the embedded parasite (such as itching, pain and restricted mobility) but also confirm the mental strain and distress it causes. Since the disease cannot be concealed in the setting where the patients live, children are exposed to ridicule and stigmatization. Besides, the impaired mobility is presumably responsible for restricted social interactions and hinders typical leisure activities of children living in rural Africa.

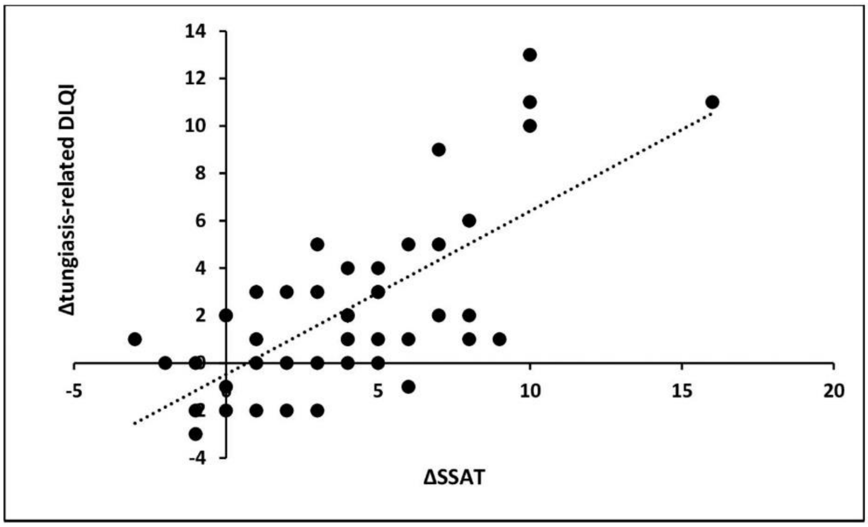

Fig 3. Correlation between individual decrease in severity of acute tungiasis (Δ SSAT) and decrease in impairment of life quality (Δ tungiasis-related DLQI) after treatment (rho = 0.61, p < 0.001); dotted line = regression curve.

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Second, the study clearly shows that a cause-effect-relationship exists between tungiasis and impaired life quality. At baseline the intensity and severity of tungiasis as well as the degree of pain were all positively correlated to the degree of life quality impairment and the degree of association was strong. After effective treatment life quality ameliorated or was restored. On the individual level there was a highly significant correlation between the reduction of disease severity and the amelioration of life quality after treatment. Finally, life quality was not restored in the patients who became re-infected during the observation period (Fig 3). Whereas in previous studies on life quality in neglected parasitic skin diseases it remained unknown to which degree the setting (such as living in poverty) contributed to the impairment categories perceived by the patients, this study convincingly shows that it is the disease—and not the setting—which causes an important impairment of life quality in children.

Third, the results of this study are a strong argument that tungiasis is an important health hazard—on the individual level as well as on the public health level—and that health care providers and regulators should give it the priority it deserves. Effective treatment and prevention do exist and should be made accessible for all patients in endemic areas [17,36].

The study has a couple of limitations: First, an observation time of four weeks is too short to completely reverse clinical pathology and, hence, it is also too short to determine whether life quality will be completely restored after all lesions have healed. However, a prolongation of the follow up period would have increased the risk of re-infection. In this case, it would have been impossible to distinguish between inflammation still persisting from an original infection and clinical pathology resulting from newly penetrated sand fleas. Second, a higher power of the study would have been preferable. However, due to financial and logistic constraints, it was impossible to increase the study size and to include a control group. Third, there is an over-representation of males in the study population. This sex imbalance reflecting the higher prevalence of tungiasis in males in the endemic areas [4, 5] might have been caused by a selection bias.

Taken together, a simple tool enabled the demonstration of a cause-effect-relationship between the presence of a wholly neglected tropical disease and impaired life quality in children living in an impoverished setting in rural Africa. This work highlights the urgent need for international donors to support the development and registration of curative and preventive interventions, and for policy makers and health officials in endemic countries to address tungiasis to avoid this suffering.

Supporting information

S1 Appendix. Database. Prevalence of tungiasis in 5 schools in Kilifi County.
(DOCX)

S2 Appendix. Visual analogue scales. Not at all = 0 points, Only a little = 1 point, Quite a lot = 2 points, Very much = 3 points.
(DOCX)

S3 Appendix. mDLQI for children tungiasis patients (5–15 y) back-translated into English from Swahili. Not at all = 0 points, Only a little = 1 point, Quite a lot = 2 points, Very much = 3 points.
(DOCX)

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PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Prevalence, intensity and risk factors of tungiasis in Kilifi County, Kenya: I. Results from a community-based study

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Abstract

Background

Tungiasis is a neglected tropical disease caused by female sand fleas (*Tunga penetrans*) embedded in the skin. The disease is associated with important morbidity. Tungiasis is endemic along the Coast of Kenya with a prevalence ranging from 11% to 50% in school-age children. Hitherto, studies on epidemiological characteristics of tungiasis in Africa are scanty.

Methods

In a cross-sectional study 1,086 individuals from 233 households in eight villages located in Kakuyuni and Malanga Sub-locations, Kilifi County, on the Kenyan Coast, were investigated. Study participants were examined systematically and the presence and severity of tungiasis were determined using standard methods. Demographic, socio-economic, environmental and behavioral risk factors of tungiasis were assessed using a structured questionnaire. Data were analyzed using bivariate and multivariate regression analysis.

Results

The overall prevalence of tungiasis was 25.0% (95% CI 22.4–27.5%). Age-specific prevalence followed an S-shaped curve, peaking in the under-15 year old group. In 42.5% of the households at least one individual had tungiasis. 15.1% of patients were severely infected ($\geq$ 30 lesions). In the bivariate analysis no specific animal species was identified as a risk factor for tungiasis. Multivariate analysis showed that the occurrence of tungiasis was related to living in a house with poor construction characteristics, such as mud walls (OR 3.35; 95% CI 1.71–6.58), sleeping directly on the floor (OR 1.68; 95% CI 1.03–2.74), the number of people per sleeping room (OR = 1.77; 95% CI 1.07–2.93) and washing the body without soap (OR = 7.36; 95% CI 3.08–17.62). The odds of having severe tungiasis were high in males (OR 2.29; 95% CI 1.18–44.6) and were very high when only mud puddles were available as a water source and lack of water permitted washing only once a day (OR 25.48 (95% CI 3.50–185.67) and OR 2.23 (95% CI 1.11–4.51), respectively).

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Conclusions

The results of this study show that in rural Kenya characteristics of poverty determine the occurrence and the severity of tungiasis. Intra-domiciliary transmission seems to occur regularly.

Author summary

Tungiasis (sand flea disease) is an ectoparasitic skin disease and belongs to the group of NTDs (Neglected Tropical Diseases). It is caused by sand fleas penetrating into the skin of the feet, causing an inflammatory reaction with pain and itching. Attempts to remove the flea with inappropriate sharp tools are painful and cause bacterial superinfection, eventually leading to restricted mobility. In resource-poor communities without access to health care, prevention is the most valuable control measure. In this study we identified important risk factors for the occurrence of tungiasis and sever disease. The most relevant risk factors were poor hygiene practices and poor housing conditions. Simple control interventions such as having solid walls and floors in the house, improved access to water and washing with soap could reduce the disease burden considerably.

Introduction

Tungiasis (sand flea disease) is a parasitic skin disease caused by female sand fleas (*Tunga penetrans)* penetrated into the skin of human or animal hosts. Tungiasis belongs to the family of neglected tropical diseases (NTDs) [1,2]. It is prevalent in resource-poor rural communities in sub-Saharan Africa, the Caribbean and South America [3–7]. Children between 5 and 14 years and the elderly bear the highest disease burden with prevalences up to 85% [7]. While the great majority of patients harbours less than 10 embedded sand fleas, single individuals may have hundreds of parasites [8,9]. Once embedded in the skin, typically of the toes, the soles and the heels [10], the flea matures. Within the period of up to five weeks it grows until it reaches the size of a pea, produces and releases eggs and finally dies [11]. Morbidity is related to an intense inflammatory response triggered by the development of sand fleas embedded in the epidermis [10,12,13]. Bacterial superinfection is common and intensifies the inflammation. Inflammation and mutilation of the feet eventually lead to impairment of mobility [12]. Main risk factors found in previous studies in Brazil and Nigeria are poor housing and the presence of animals on the compound [14,15]. Awareness of the public health importance of tungiasis has been growing in Kenya in recent years, but valid data on epidemiological characteristics do not exist. In order to develop a sustainable control program for tungiasis in resource-poor communities along the Kenyan Coast, two population-based studies were performed: one in households and the other in schools. Here, we report the results of the household-based study.

Materials and methods

Ethics statement

The study was approved by the Ethics Review Committee at Pwani University, Kilifi County, Kenya; approval number ERC/PhD/010/2014. The custodians and their protégés were informed about the objectives and procedures of the study in their mother language (Giriama or Swahili) by a Community Health Worker (CHW). The right to deny participation and withdraw consent at any given time was clearly explained.

The informed consent form was read out loud word by word in Giriama or Swahili and explained further when required, before any interviews were conducted. Questions of the custodian and the children were discussed and answered by a CHW. Consent was obtained via fingerprint or signature from the legal guardian. The examination was performed in a protected surrounding to guarantee the privacy of the patient. Children and adolescents were only examined in the presence of their caregiver.

Any individuals found to have tungiasis were referred to the local CHWs for treatment and follow up according to their standard protocols which have been approved for use by the Ministry of Health at national and county level. For other illnesses requiring treatment a referral form was prepared by a CHW, and patients were referred to the nearest Health Facility. Washing and treatment were also made available for compound members with tungiasis who did not participate in the study.

The information provided to the households verbally is included as supplementary electronic information along with the consent form which was to be signed (S1 Appendix).

Study area and study population

The study was performed in eight villages located in Kakuyuni and Malanga Sub-locations of Malindi Sub-county, Kilifi County, eastern Kenya, in the dry season from August to October 2014. In the area tungiasis is endemic with prevalences ranging from 30 to 85% in school age children (S2 Appendix).

In Malindi Sub-county rural communities are small and consist of clusters of two to five houses separated by bush or farm land. The area is divided into two ecological zones: Kakuyuni Sub-location, a very densely populated area in the coastal strip with homesteads located side by side. It has a tropical climate with an average annual rainfall of 1,200 mm, temperatures ranging from 28–34°C and high humidity most of the year. Malanga Sub-location is located inland and is much drier with average annual rainfall of 400 mm. Homesteads are located about 100 m from each other in this area. There are two rainy seasons: one between March and May and the other between October and November, interspersed with dry seasons.

Malindi Sub-county has a population of 272,000 with 42.3% being under 15 years of age. The population included in the survey are entirely of the Giriama tribe. While 55% of households have access to piped water and 60% to improved sanitation, only 17% have access to electricity (Malindi Public Health Office 2015). Many of the people live in mud-walled houses with a thatch roof and sandy floor (First Kilifi County Integrated Development Plan 2013–2017). For Kilifi County as whole the poverty rate (i.e. < 1 US$ per day) is 71.4% (http://www.crakenya.org/county/kilifi/). The majority of the population in the study area practice subsistence agriculture, charcoal burning and small scale businesses. The main foodstuffs cultivated are maize, cassava, coconuts, and mangoes.

Study design

The study was a cross-sectional survey of a random sample of households in Kakuyuni and Malanga Sub-locations, Kilifi County, Kenya. These sublocations were selected because no intervention against tungiasis had been performed so far.

For this study a household was classified as a single structure/house. Since most people live in homesteads of extended families, sharing eating, washing and sanitation facilities, we selected one structure/house per homestead in a standardized manner, always choosing the first house on the left when entering the compound.

Individuals of any age and sex were eligible for participation as long as they had spent at least 4 nights per week in the selected household for the last three months. To be included, a household needed to have someone over the age of 18 present at the time of the visit to sign the consent forms and respond to the interview questions.

During the preparation phase contact was made with the County and District leadership in both the Ministry of Health and the Ministry of Education, the Zonal Education Officer and the Community Health Officers to obtain their approvals and support for the study. We held meetings with all CHWs in each **S**ub-location, gave specific training on tungiasis and explained the aims and procedures of the study, emphasizing that participation was completely voluntary and subjects had the opportunity to withdraw from the study at any point of time.

The study was carried out between August 13 and October 5, 2014, i. e. during a dry season. A total of 1,086 individuals from 233 households in eight villages were included in the study.

Data were collected through a door-to-door survey of the selected households with the help of local CHWs. Eligible patients were explained the procedure and were asked for consent. In case of minors a caregiver (usually the mother) was asked to provide informed consent. If household members were not present during our first visit, we returned to the house on one further occasion. Individuals who could not be reached at home during the second visit were invited to come to the local health facility within the next days. Household members who could not be examined on any occasion were not included in the study.

In order to identify risk factors for the occurrence of tungiasis and severe disease, we requested information about demographic, socio-economic, environmental and behavioural characteristics of the individuals and the household. Structured interviews were conducted with the head of household (usually the mother) using a pre-tested questionnaire in Giriama or Swahili. Environmental, socioeconomic and some behavioural risk factors were assessed at the household level, other risk factors were assessed on the individual level.

Since cash flow does not correctly indicate the economic status of a household in low-income communities [16,17], we used an asset score similar to the one previously established for cutaneous larva migrans, another neglected tropical skin disease associated with poverty [18]. The score is composed of the following assets:

Presence in the household of a radio (2 points), television (5 points), fridge (5 points), gas/solar lamp (1 point); possession of at least one mobile phone (1 point), bicycle (3 points) and motor bike (10 points). The score can vary between 0 and 27 points.

For the diagnosis of tungiasis, the feet of the patients were carefully washed with soap in a basin. Each individual was examined for tungiasis based on a standardized procedure [3]. Since a high number of lesions at the feet frequently coincides with the presence of ectopic lesions at the hands [19], we also systematically examined the hands of the patients. Patients were also asked whether they had tungiasis lesions in other regions of the body. Lesions were staged according to the Fortaleza classification and counted [11]:

- stage I: penetrating sand flea
- stage II: brownish/black dot with a diameter of 1–2 mm surrounded or not by an erythema
- stage III: circular yellow-white watch glass-like patch with a diameter of 3–10 mm and with a central black dot
- stage IV: brownish-black crust with or without surrounding necrosis

Stage I to III are viable sand fleas; in stage IV the parasite is dying or already dead [11] Lesions manipulated with a sharp instrument (by the patient or their caregiver) with the intention to remove the embedded parasite were documented as manipulated lesions. Based on the number of lesions present, the intensity of tungiasis was classified as light (1–5 lesions), moderate (6–30 lesions) or high (>30 lesions) [14].

Statistical analysis

The data were entered into an Excel database (Excel Version 2013, Microsoft, Redmont, Washington, USA), checked for errors which might have occurred during data entry and then transferred to SPSS (PASW Statistics 18.0, SPSS Inc., Chicago, IL, USA). The data analysis was carried out using the Analysis ToolPack Add-In (Microsoft, Redmont, Washington, USA). Graphs were created with the PowerPivot Add-In (Microsoft, Redmont, Washington, USA). Relative frequencies were compared with the Chi-square test and Fisher's exact test. The Spearman rank correlation coefficient was calculated to determine the significance of correlations. Odds ratios together with their 95% confidence interval (CI) were calculated first in a bivariate analysis. In a second step, variables which were significantly ($p < 0.05$) related to the occurrence of tungiasis and/or severe disease were entered in a multivariate logistic regression model with stepwise forward inclusion of variables to identify independent exposure variables. Factors which showed up as significant in the bivariate analysis but were assessed only in individuals older than 18 were not included in the logistic regression model. For risk factors suitable for an intervention, population attributable fractions (PAF) were calculated. The PAF, calculated as % exposed among cases x attributable risk (AR), is the fraction of cases which would not have occurred if an exposure had been avoided, assuming the exposure is causal and the other risk factors in the population remain unchanged. AR is calculated as (OR– 1)/OR and is the risk of tungiasis in the exposed group due to the exposure. The sample size of this study was estimated based on field studies performed in Brazil and Nigeria and contained the following assumptions: control-case-ratio 1:3; hypothetical proportion of controls with exposure 30%; least detectable odds ratio 1.75; power of the test 0.90; confidence level 0.95. This would require 205 cases and 610 controls. To account for uncertainties and drop out we attempted to include a sample of 1000 individuals.

Results

Characteristics of the study population

Of the 239 homesteads visited 233 fulfilled the criterion of having an inhabited first house on the left. Of the 1,203 individuals living in these households, 114 (72 males and 42 females) were not encountered on any of the visits, reducing the study population to 1,089. Of these, three did not fulfil the inclusion criterion of having spent at least four nights per week in the selected homestead during the last three months. Thus, the number of individuals available for the assessment of risk factors was 1,086, all of which agreed to being interviewed and examined (Fig 1). Three hundred and twenty four patients (70 households) were recruited from Kakuyuni, 221 (41) from Goshi, and 172 (43) from Vihingoni community in Kakuyuni Sub-location; 116 (24) from Mtoroni, 27 (5) from Yembe, 133 (28) from Kadzitsoni, 76 (18) from Chembe and 17 (4) from Bahati community in Malanga Sub-Location.

The study population comprised 57.3% females, and 58.6% under the age of 15 years. Of those over 18 years, 54.1% reported being Christians while 19.6% were Muslims, 31.4% were illiterate and a further 34% had not completed primary school education. The majority of houses (89%) had dirt floors and mud walls (84.5%), did not have improved latrines (56.7% used the bush, 32.6% used traditional latrines) and shared community taps for their source of water (83.7%) (Tables 1 and 2).

The overall prevalence of tungiasis in the study population was 25.0% (95% CI 22.4–27.5%), but in 42.5% of the households at least one individual had tungiasis. Of those with tungiasis,

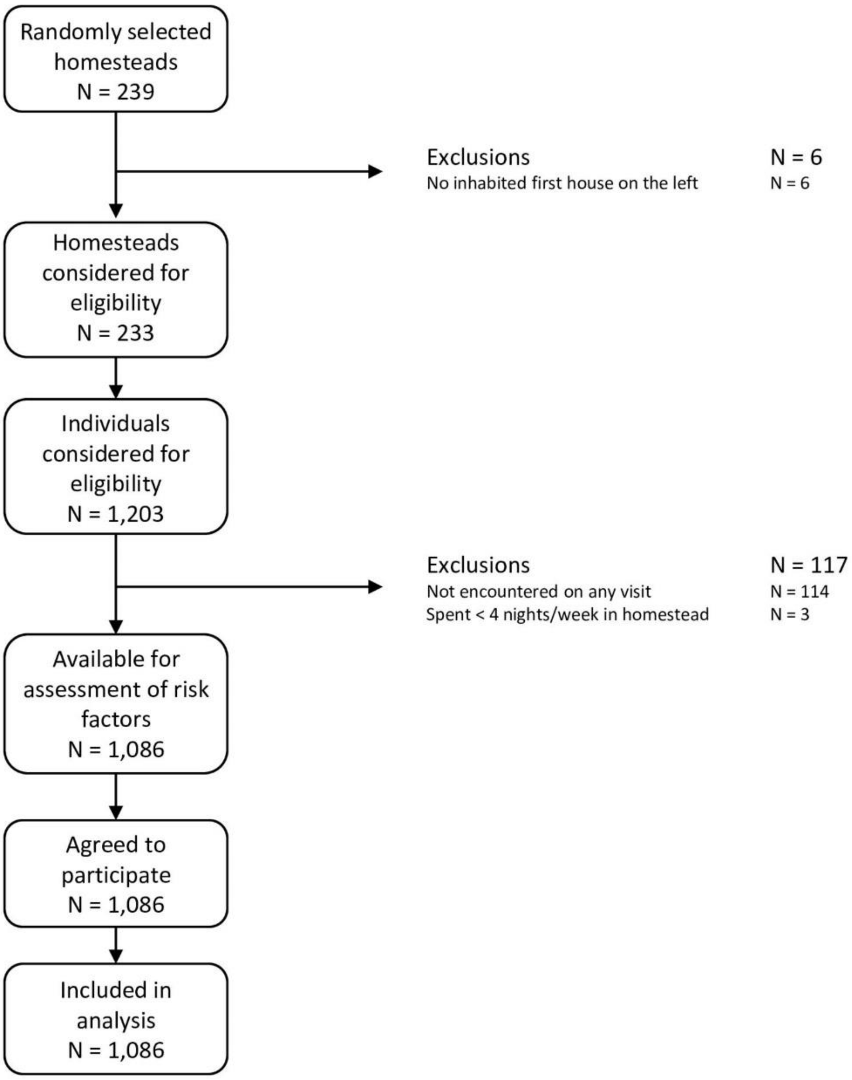

Fig 1. Flow chart of study population.

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52.8% had a light (1 to 5 lesions), 32.1% a moderate (6 to 30 lesions) and 15.1% a high intensity of infection (>30 lesions). Five percent of the patients had ectopic lesions, almost exclusively on the hands. Age-specific prevalences and intensity of infection are shown in Fig 2. There was a tendency of higher occurrence of tungiasis in elderly individuals living alone, although it was not significant (p = 0.2111). In 14 single-person households there were two adults < 40 years without tungiasis, six 40 to 59 year olds of whom 2 had tungiasis and six > 60 year olds of whom 4 had a mild to severe tungiasis. The prevalence of infection and high intensity of infection correlated significantly (Fig 3) (rho = 0.90, p = 0.0059), with the highest prevalence being in the under 15 year olds and over 40 years. The youngest patient was four months old, 4 patients were younger than one year, while the oldest patient was 80 years old.

Table 1. Demographic characteristics of the study population (n = 1,086 individuals).

Characteristic	Frequency	(%)
Sex		
Female	622	57.3
Male	464	42.7
Age (years)		
0–4	211	19.4
5–9	245	22.6
10–14	180	16.6
15–19	80	7.4
20–39	189	17.4
40–59	114	10.5
$\geq$ 60	64	5.9
n.k.	3	0.3
Village		
Kakuyuni	324	29.8
Goshi	221	20.3
Vihingoni	172	15.8
Mtoroni	116	10.7
Yembe	27	2.5
Kadzitsoni	133	12.2
Chembe	76	7.0
Bahati	17	1.6
Religion[a]		
None	19	4.9
Muslim	76	19.6
Christian	210	54.1
Traditionist	76	19.6
n.k.	7	1.8
Education[a]		
Illiterate	122	31.4
Primary school not completed	132	34.0
Primary school completed	133	34.3
n.k.	1	0.3
Occupation[a]		
Unemployed	89	22.9
Farmer	179	46.1
Other occupation	113	29.1
n.k.	7	1.8

[a] information on religion, education and occupation were only collected for adults $\geq$ 18 years (n = 381)
n.k. = not known

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Risk factor analysis

Prevalence and severity of tungiasis varied considerably between the villages with Yembe and Bahati having a prevalence of 59.3% and 64.7% respectively, while Mtoroni and Vihingoni had prevalences of 7.8% and 13.4% (Table 3). Residence in Yembe and Bahati was a significant risk factor for tungiasis (OR 17.3 and 21.8 respectively, p<0.0001) and in Kakuyuni for both occurrence of tungiasis (OR 6.5, p<0001) and severe tungiasis (OR 9.2, p<0.05). Tables 3 to 5 show

Table 2. Socio-economic characteristics of the study population (n = 233 households).

Characteristic	Frequency	(%)
Housing		
Type of floor material		
Cement/stone	26	11.2
Smeared mud	136	58.4
Sand/dust	70	30.0
Mixed mud and sand	1	0.4
Type of wall material		
Stone	31	13.3
Mud	197	84.5
Mixed stone and mud	5	2.1
Type of roof material		
Makuti[a]	112	48.1
Mabati[b]	118	50.6
Mixed makuti and mabati	1	0.4
Tiles	2	0.9
Sanitation		
Toilet		
Flush toilet	10	4.3
Ventilated pit latrine	15	6.4
Traditional latrine	76	32.6
Bush	132	56.7
Waste disposal		
Pit	85	36.5
Pile	100	42.9
Spread	47	20.2
Compost	1	0.4
Water source		
Tap on compound	36	15.5
Shared community tap	195	83.7
Mud puddles	2	0.9
Time to reach water source (min)		
0–4	73	31.3
5–9	53	22.7
10–14	42	18.0
15–19	20	8.6
20–29	12	5.2
$\geq$ 30	33	14.2
Healthcare		
Time to reach next health facility (min)		
0–9	16	6.9
10–19	40	17.2
20–29	43	18.5
30–39	70	30.0
40–49	16	6.9
50–59	2	0.9
$\geq$ 60	46	19.7
Economic status		

(*Continued*)

Table 2. (*Continued*)

Characteristic	Frequency	(%)
Monthly income per household (KSh)[c]		
0–4850	87	37.3
> 4850	40	17.2
n.k.	106	45.5
Number of meals per day		
1	6	2.6
2	62	26.6
> 2	165	70.8
Land ownership		
Own	228	97.9
Rent	3	1.3
Squatt	2	0.9
Domestic animals		
Animals on compound		
Any animal	205	88.0
Dogs	59	25.3
Cats	59	25.3
Goats	140	60.1
Cows	70	30.0
Chicken	172	73.8
Ducks	42	18.0

[a] palm leaves
[b] corrugated iron sheets
[c] KSh 4850 correspond to the minimum wage in Kenya for an unskilled worker in agricultural industry at the time of the survey and is equivalent to ~ 55 USD
n.k. = not known

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demographic, socio-economic, behavioral, environmental and geographic risk factors in the bivariate analysis.

The bivariate analyses identified many risk factors for tungiasis (Table 4). These included being of male sex (OR = 1.59, p = 0.001) and age < 15 and ≥ 40 years (OR between 4.04 and 12.45, p<0.001 and p<0.01, respectively). Living in a house with a floor of sand/earth (OR = 4.31, p < 0.0001) and mud walls (OR = 4.11, p < 0.0001) were significantly related to the occurrence of tungiasis. Other significant risk factors were: using a traditional latrine or bush as a toilet; spreading waste on the compound or disposing waste on a pile; using mud puddles as a water source (all p < 0.05); a low frequency of washing (only once a day, OR = 1.99, p<0.0001) and not using soap (OR = 3.81, p<0.001); living in crowded houses (4–6 persons per household, OR = 1.69, p < 0.05); sleeping together with many other persons in a room (p < 0.001) or children sleeping on the floor (OR = 1.89, p < 0.001). In individuals 18 years or older, not completing primary school or never having attended primary school at all increased the odds of being affected by tungiasis by a factor of three (OR = 3.37, p<0.05, Table 5).

On conducting the multivariate analyses, only the demographic exposure variables male sex and age under 15 remained highly significant (Table 6). Exposure variables indicating a low economic status such as poor construction characteristics of the house, direct sleeping on the

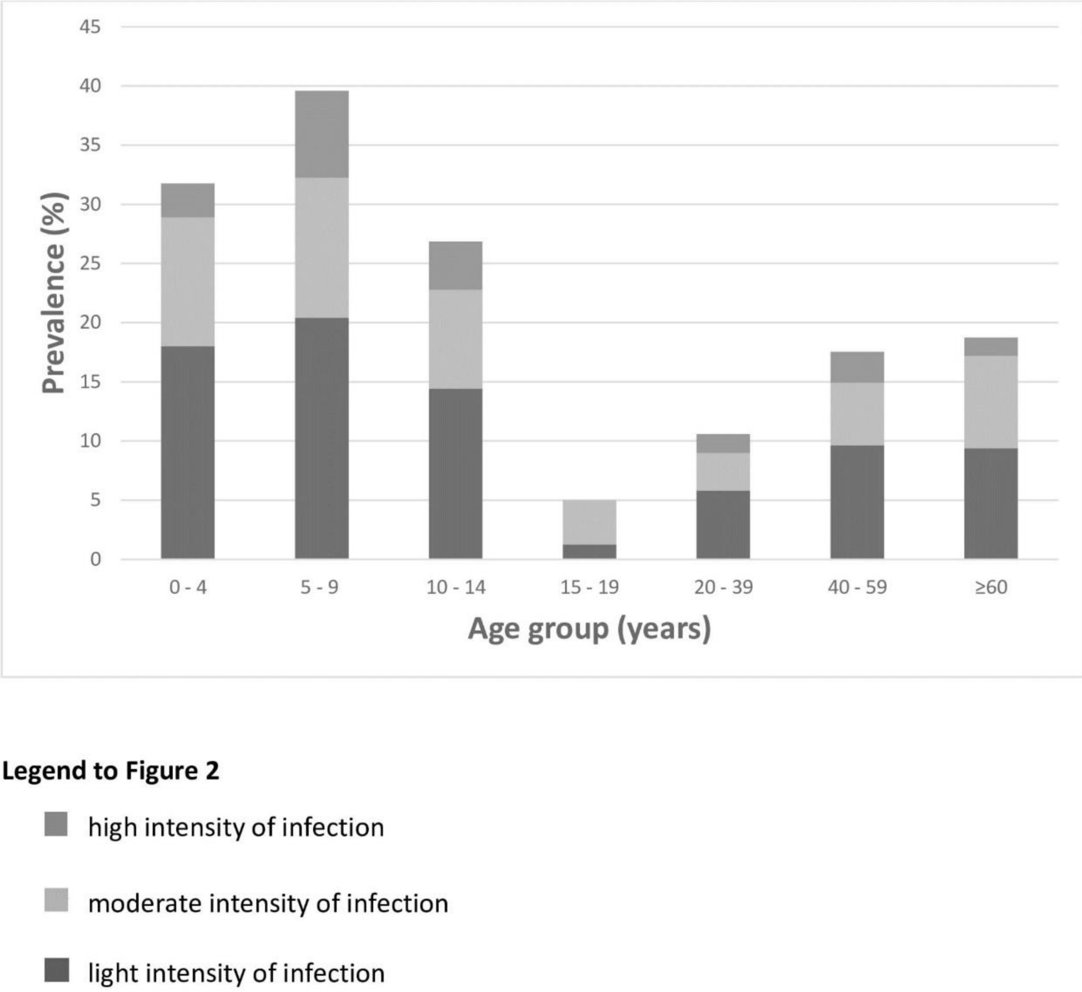

Fig 2. Age-specific prevalence and intensity of tungiasis in the study area. Column heights indicate overall prevalence in age groups.

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floor, many people sleeping in a single room and restricted access to water also remained as significant factors.

Population Attributable Fractions were calculated for those variables which are amenable to modification (Table 7). The PAF for living in a house with mud walls was 64.45%, for washing without soap 16.61% and washing only once a day 20.18%.

Discussion

Tungiasis is a NTD prevalent in resource-poor communities in South America, the Caribbean and sub-Saharan Africa [3–7]. Although the disease is associated with important morbidity, it is neglected by health care providers globally [2,20–23]. Widespread control has never been attempted, only isolated efforts to treat infected individuals, often by non-governmental

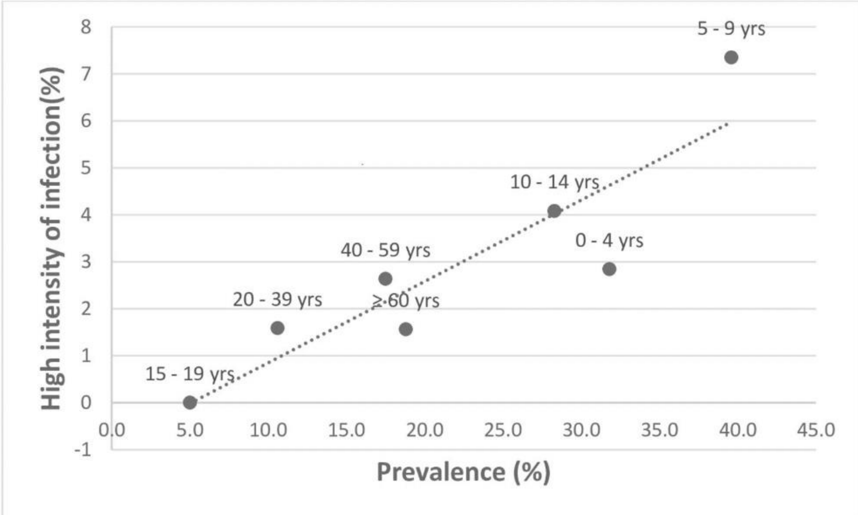

Fig 3. Correlation between age-specific prevalence and age-specific frequency of high intensity of infection (> 30 lesions); rho = 0.90, p = 0.006.

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organizations. In East Africa, this is largely due to the lack of data on prevalence and severity of disease and hitherto risk factors have only been investigated in restricted age groups.

This study showed a prevalence of 25% in the overall study population and 33.8% in children under 15 years. The overall prevalence is similar to that found in a community-based study in Central Uganda (where the median prevalence in humans was 22%, but only animal keeping households were included), but considerably lower than prevalences observed in rural and urban resource-poor communities in Brazil and Nigeria (with prevalences up to 45%) [6,7,20,24,25]. Age-specific prevalence followed an S-shape curve, peaking in the 5 to 9 year age group and the elderly, an unusual epidemiological characteristic which seems to be true for all geographic areas and independent of the overall prevalence [6,7,15,21]. This may be due to certain age-specific behavioural patterns associated with different degrees of exposure, e.g.

Table 3. Bivariate analysis of geographic risk factors (n = 1,086 individuals).

Exposure variable		n	Frequency of tungiasis		Presence of tungiasis		Presence of severe Tungiasis (> 30 lesions)	
			(%) any	(%) heavy	OR (95% CI)	P value	OR (95% CI)	P value
Location								
Malanga Sublocation[a]	Mtoroni	116	7.8	0.9	Reference			
	Yembe	27	59.3	3.7	17.29 (6.20–48.23)	**<0.0001**	4.42 (0.27–73.05)	0.2987
	Kadzitsoni	133	33.8	3.8	6.08 (2.82–13.12)	**<0.0001**	4.49 (0.52–30.02)	0.1732
	Chembe	76	10.5	0.0	1.40 (0.51–3.80)	0.5106	0.50 (0.02–12.52)	0.6754
	Bahati	17	64.7	0.0	21.80 (6.53–72.74)	**<0.0001**	2.20 (0.09–56.17)	0.6334
Kakuyuni Sublocation	Kakuyuni	324	35.5	7.4	6.54 (3.19–13.40)	**<0.0001**	9.20 (1.23–68.80)	**0.0306**
	Goshi	221	19.9	2.7	2.96 (1.39–6.30)	**0.0050**	3.21 (0.38–26.98)	0.2831
	Vihingoni	172	13.4	2.3	1.84 (0.82–4.12)	0.1416	2.74 (0.30–24.81)	0.3704

[a] The village with the lowest prevalence was used as reference.

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Table 4. Bivariate analysis of demographic, housing, economic and behavioral risk factors (n = 1,086).

Exposure variable		n	Frequency of tungiasis		Presence of tungiasis[a]		Presence of severe tungiasis (> 30 lesions)	
			(%)any	(%)heavy	OR (95% CI)	P value	OR (95% CI)	P value
Demographic characteristics								
Sex	Female	622	21.2	2.4	Reference			
	Male	464	30.0	5.6	1.59 (1.20–2.09)	**0.001**	2.40 (1.26–4.59)	**0.008**
Age group (years)	0–4	211	31.8	2.8	8.84 (3.10–25.17)	**<0.001**	5.09 (0.28–91.45)	0.27
	5–9	245	39.6	7.3	12.45 (4.41–35.15)	**<0.001**	13.09 (0.78–219.77)	0.07
	10–14	180	28.3	5.6	7.51 (2.61–21.60)	**<0.001**	9.92 (0.57–171.31)	0.11
	15–19	80	5.0	0.0	Reference			
	20–39	189	10.6	1.6	2.25 (0.74–6.80)	0.15	3.02 (0.15–59.17)	0.47
	40–59	114	17.5	2.6	4.04 (1.33–12.33)	**0.01**	5.05 (0.26–99.21)	0.29
	≥60	64	18.8	1.6	4.38 (1.34–14.35)	**0.01**	3.80 (0.15–94.95)	0.42
Persons per household	1–3	148	18.2	4.7	Reference			
	4–6	453	27.4	4.2	1.69 (1.06–2.69)	**0.03**	0.88 (0.36–2.14)	0.78
	≥7	485	24.7	3.1	1.47 (0.93–2.35)	**0.10**	0.64 (0.26–1.61)	0.34
Children/household	0–3	454	23.6	2.9	Reference			
	4–5	324	24.4	4.9	1.05 (0.75–1.46)	0.79	1.76 (0.84–3.72)	0.13
	≥6	308	27.6	3.9	1.24 (0.89–1.72)	0.21	1.38 (0.62–3.06)	0.43
Adults/household	0–1	224	29.9	6.3	1.65 (0.89–3.07)	0.11	10.81 (0.64–183.47)	0.09
	2–3	784	24.0	3.4	1.22 (0.69–2.17)	0.49	5.70 (0.34–94.35)	0.22
	≥4	78	20.5	0.0	Reference			
Housing								
Type of floor material	Cement/stone	129	11.6	0.0	Reference			
	Smeared mud	661	22.7	4.2	2.23 (1.26–3.94)	**0.005**	11.65 (0.71–192.08)	0.08
	Sand/dust	293	36.2	4.4	4.31 (2.39–7.76)	**<0.0001**	12.47 (0.74–211.31)	0.08
Type of wall material	Stone	153	8.5	0.0	Reference			
	Mud	901	27.6	4.6	4.11 (2.29–7.40)	**<0.0001**	14.81 (0.91–241.97)	0.06
	Mixed	32	28.1	0.0	4.21 (1.62–10.98)	**0.003**	4.72 (0.09–242.42)	0.43
Type of roof material	Mabati	553	21.9	1.4	Reference			
	Makuti	519	28.7	6.4	1.44 (1.09–1.90)	**0.01**	4.36 (2.12–10.11)	**0.0001**
	Both	7	0.0	0.0	0.24 (0.01–4.18)	0.32	4.38 (0.23–81.08)	0.33
	Other	7	14.3	0.0	0.60 (0.07–4.99)	0.63	4.38 (0.23–81.08)	0.33
Location of kitchen	Outside the house	757	25.8	3.6	Reference			
	Inside the house	329	23.1	4.3	0.87 (0.64–1.17)	0.35	1.20 (0.62–2.32)	0.58
Number of sleeping rooms	≥4	68	13.2	0.0	Reference			
	3	179	20.7	2.8	1.71 (0.78–3.76)	0.18	4.32 (0.24–79.15)	0.32
	2	435	23.2	2.3	1.98 (0.95–4.14)	0.07	3.38 (0.20–58.36)	0.40
	1	404	30.7	6.4	2.90 (1.40–6.04)	**0.004**	9.59 (0.58–159.27)	0.11
Persons/sleeping room	<3	403	18.4	2.2	Reference			
	3–4	366	24.3	1.9	1.43 (1.01–2.02)	**0.04**	0.85 (0.31–2.32)	0.75
	4,5–6	195	33.8	8.7	2.27 (1.54–3.36)	**<0.0001**	4.18 (1.83–9.56)	**<0.001**
	≥7	122	34.4	6.6	2.33 (1.49–3.66)	**<0.001**	3.07 (1.16–8.14)	**0.02**
Sleeping situation of children	Raised bed[a]	910	23.2	2.9	Reference			
	Floor	146	36.3	8.2	1.89 (1.30–2.74)	**<0.001**	3.04 (1.50–6.18)	**0.002**
	Taking turns	30	23.3	10.0	1.01 (0.43–2.38)	0.98	3.78 (1.08–13.25)	**0.04**
Sanitation								

(*Continued*)

Table 4. (*Continued*)

Exposure variable		n	Frequency of tungiasis		Presence of tungiasis[a]		Presence of severe tungiasis (> 30 lesions)	
			(%)any	(%)heavy	OR (95% CI)	P value	OR (95% CI)	P value
Water source	Tap on compound	159	22.0	3.8	Reference			
	Shared community tap	918	24.9	3.6	1.18 (0.79–1.76)	0.42	0.95 (0.39–2.31)	0.91
	Mud puddles	9	77.8	22.2	12.40 (2.46–62.39)	**0.002**	7.29 (1.24–42.80)	**0.003**
Toilet	Flush toilet	36	5.6	0.0	Reference			
	Ventilated pit latrine	88	17.0	0.0	3.49 (0.76–16.14)	0.11	0.41 (0.01–21.18)	0.65
	Traditional latrine	314	25.8	4.8	5.91 (1.39–25.15)	**0.01**	3.78 (0.22–64.48)	0.35
	Bush	648	26.7	4.0	6.19 (1.47–26.05)	**0.01**	3.11 (0.19–52.02)	0.43
Waste disposal	Pit	415	24.1	1.9	Reference			
	Pile	465	23.7	4.7	0.98 (0.72–1.33)	0.87	2.53 (1.11–5.74)	**0.03**
	Spread	199	30.7	5.5	1.39 (0.96–2.03)	0.08	2.98 (1.18–7.52)	**0.03**
	Compost	7	0.0	0.0	0.21 (0.01–3.70)	0.28	3.20 (0.19–60.59)	0.43
Time to reach water source (min)	0–4	341	25.2	4.4	Reference			
	5–9	272	29.8	5.5	1.26 (0.88–1.80)	0.21	1.27 (0.61–2.64)	0.53
	10–14	202	21.8	3.0	0.83 (0.55–1.25)	0.36	0.67 (0.25–1.74)	0.41
	15–19	79	19.0	0.0	0.69 (0.38–1.28)	0.24	0.13 (0.01–2.24)	0.16
	20–29	46	23.9	8.7	0.93 (0.45–1.92)	0.85	2.07 (0.66–6.53)	0.21
	≥30	146	23.3	0.7	0.90 (0.57–1.42)	0.65	0.15 (0.02–1.15)	0.07
Frequency of washing	Twice a day	828	21.7	3.0	Reference			
	Once a day	236	35.6	6.4	1.99 (1.45–2.72)	**<0.0001**	2.18 (1.13–4.21)	**0.02**
	Less often	22	31.8	4.5	1.68 (0.67–4.18)	0.27	1.53 (0.20–11.82)	0.68
Use of soap	Always	566	22.8	3.2	Reference			
	Sometimes	486	25.5	4.3	1.16 (0.87–1.54)	0.30	1.37 (0.72–2.61)	0.33
	Never	34	52.9	5.9	3.81 (1.89–7.69)	**<0.001**	1.90 (0.42–8.56)	0.40
	Always	566	22.8	3.2				
Economic status								
Income per capita (KSh/month)[b]	>3400	25	12.0	0.0	Reference			
	1000–3400	166	18.1	1.2	1.62 (0.45–5.76)	0.46	0.78 (0.04–16.61)	0.87
	<1000	414	27.1	2.9	2.72 (0.80–9.26)	0.11	1.58 (0.09–27.52)	0.75
	n.k.	481	26.2	5.6	2.60 (0.77–8.85)	0.13	3.09 (0.18–52.04)	0.43
Asset score	0–4	761	27.2	4.3	7.85 (1.05–58.71)	**0.04**	2.07 (0.12–34.85)	0.61
	5–15	303	20.8	2.6	5.51 (0.73–41.77)	0.10	1.29 (0.07–23.16)	0.86
	≥16	22	4.5	0.0	Reference			
Number of meals/day	>2	773	23.7	3.5	Reference			
	2	291	27.8	4.1	1.24 (0.92–1.69)	0.16	1.19 (0.59–2.38)	0.63
	1	22	31.8	9.1	1.50 (0.60–3.75)	0.38	2.76 (0.61–12.43)	0.19

[a] Bed height was not assessed systematically, but was approximately 45 cm above the ground (personal observation)

[b] KSh 4850 correspond to the minimum wage in Kenya for an unskilled worker in agricultural industry at the time of the survey and is equivalent to ~ 55 USD

n.k. = not known

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young children playing on the ground, as suggested by Muehlen et al. [6] and the elderly spending large amounts of time lying on the ground. Other hypotheses are a protecting effect of the increasing corneal layer of the feet [26,27], a higher level of practice and dexterity in taking out embedded sandfleas with increasing age [7] and more attention given to personal hygiene.

Table 5. Bivariate analysis of educational, occupational and environmental risk factors (n = 1,086).

Exposure variables		n	Frequency of tungiasis		Presence of tungiasis		Presence of severe tungiasis (> 30 lesions)	
			% (any)	(%) heavy	OR (95% CI)	p-value	OR (95% CI)	p-value
Education[a]	Primary school completed	133	6.8	0.8	Reference			
	Primary school not completed	132	15.9	3.8	2.61 (1.15–5.93)	**0.02**	5.20 (0.60–45.10)	0.14
	Illiterate	122	19.7	0.8	3.37 (1.50–7.59)	**0.003**	1.09 (0.07–17.63)	0.95
Occupation[a]	Other occupation	113	8.8	0.9	Reference			
	Farmer	179	15.6	1.1	1.91 (0.89–4.10)	0.10	1.27 (0.11–14.12)	0.85
	Unemployed	89	15.7	4.6	1.92 (0.81–4.56)	0.14	5.27 (0.58–48.02)	0.14
Religion[a]	None	19	26.3	0.0	Reference			
	Muslim	76	5.3	0.0	0.16 (0.04–0.65)	**0.01**	0.25 (0.00–13.26)	0.50
	Christian	210	13.3	1.0	0.43 (0.14–1.29)	0.13	0.47 (0.02–10.09)	0.63
	Traditionist	76	21.1	6.6	0.75 (0.23–2.38)	0.62	3.00 (0.16–56.64)	0.46
Presence of domestic animals on compound	Dogs Yes	300	26.3	4.3	1.11 (0.82–1.50)	0.52	1.23 (0.63–2.40)	0.55
	No	786	24.4	3.6	Reference			
	Cats Yes	260	26.5	3.5	1.12 (0.81–1.53)	0.50	0.89 (0.42–1.89)	0.76
	No	826	24.5	3.9	Reference			
	Goats Yes	633	28.3	3.9	1.55 (1.16–2.06)	**0.003**	1.12 (0.59–2.13)	0.72
	No	453	20.3	3.5	Reference			
	Cows Yes	339	28.3	3.8	1.29 (0.97–1.73)	0.08	1.02 (0.52–2.00)	0.94
	No	747	23.4	3.7	Reference			
	Chicken Yes	801	24.3	3.9	0.88 (0.65–1.20)	0.44	1.11 (0.54–2.29)	0.79
	No	285	26.7	3.5	Reference			
	Ducks Yes	215	25.6	4.7	1.04 (0.74–1.47)	0.81	1.32 (0.64–2.74)	0.45
	No	871	24.8	3.6	Reference			
Access to health care								
Time to reach the nearest health facility (min)	0–9	70	37.1	11.4	Reference			
	10–19	192	21.9	2.1	0.47 (0.26–0.86)	**0.01**	0.16 (0.05–0.57)	**0.004**
	20–29	184	28.8	7.6	0.68 (0.38–1.22)	0.20	0.64 (0.26–1.60)	0.33
	30–59	436	23.9	2.1	0.53 (0.31–0.90)	**0.02**	0.16 (0.06–0.44)	**0.001**
	≥60	204	22.5	2.9	0.49 (0.27–0.88)	**0.02**	0.23 (0.08–0.70)	**0.01**

[a] calculated for individuals ≥18 years (n = 388)

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Table 6. Risk factors of tungiasis/severe tungiasis after multivariate analysis.

	Presence of tungiasis		Presence of severe tungiasis (> 30 lesions)	
	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Being of male sex			2.29 (1.18–4.46)	0.01
Age				
0–4	8.90 (2.94–26.89)	<0.0001		
5–9	12.88 (4.31–38.54)	<0.0001		
10–14	7.23 (2.37–22.02)	<0.0001		
40–59	3.49 (1.07–11.39)	0.04		
≥ 60	5.32 (1.50–18.85)	0.01		
Using mud puddles as water source			25.48 (3.50–185.67)	0.001
Washing only once a day			2.23 (1.11–4.51)	0.03
Using soap when washing:				
sometimes	1.57 (1.09–2.28)	0.02		
never	7.36 (3.08–17.62)	<0.0001		
Staying in a house with:				
4.5–6 persons/sleeping room	1.77 (1.07–2.93)	0.03		
children sleeping on the floor	1.68 (1.03–2.74)	0.04		
Time to health facility 10–19 min	0.47 (0.23–0.95)	0.04	0.20 (0.06–0.69)	0.01
30–59 min			0.12 (0.04–0.34)	<0.0001
≥ 60 min			0.22 (0.07–0.68)	0.009
Living in a house with mud walls	3.35 (1.71–6.58)	<0.0001		

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More than half of all cases (52.8%) had a low intensity of infection (less than 6 lesions), while 15% had more than 30 lesions. The percentage of patients with severe tungiasis was lower than observed in Brazil [7,15,20,24,25]. However, this is not surprising, taking into account that prevalence and intensity of infection are positively correlated [6,21,28]. The observation that age-specific prevalence significantly correlated to high intensity of infection (rho = 0.90; Fig 3) confirms that children and the elderly bear the highest burden of disease. Anecdotal reports show that elderly individuals without social support structures tend to be infected with tungiasis more frequently [21]. This tendency was confirmed in this study, although it was not significant.

Tungiasis is a zoonosis in which sylvatic, peri-domiciliary and domestic cycles are interlinked in a complex manner [2]. The situation becomes even more intricate when transmission also occurs inside the house, without the involvement of an animal reservoir. Intra-domiciliary transmission indicates that the off-host cycle of *T. penetrans* is completed inside the house.

Table 7. Population attributable fractions for exposure variables amenable to modification.

	AR (%)	% exposed among cases	PAF (%)
Washing only once a day	55.16	36.6	20.18
Not using soap when washing	36.31	45.8	16.61
Staying in a house with mud walls	70.15	91.9	64.45

PAF is the fraction of cases which would not have occurred if an exposure had been avoided and is calculated as % exposed among cases x attributable risk (AR).
AR is the risk of tungiasis in the exposed group due to the exposure and is calculated as (OR– 1)/OR.

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Usually, this is a room in which family members spend many hours a day, such as the sleeping room. If the floor in this room consists of sand, dried mud or rugged cement with holes and cracks, eggs that have been expelled by embedded female sand fleas overnight and which have fallen on the floor are swept into crevices of the floor or into the cracks between floor and wall, when the room is cleaned with a broom in the morning. Eggs can develop into larvae and pupae in such cracks [29].

That intra-domiciliary transmission occurs in the study area is supported by the finding that direct sleeping on the floor or if walls of the sleeping room consisted of mud remained significant risk factors in the multivariate analysis. The more people slept in a room the higher were the odds of tungiasis in household members.

It is known that different animal species act as reservoirs in different countries [25,30,31]. In our study population, 74% of all households had chicken, 60% had goats, 25% had dogs and 25% had cats. However, no specific animal species was identified as a risk factor for tungiasis in this study. This finding supports the assumption that perhaps in these coastal communities the *Tunga penetrans* cycle is almost entirely human and does not involve animal reservoirs. It should be noted that animals were not examined for infection in this study, only observed as present in the compound and reported as to where they sleep at night (S3 Appendix). In Northeast Brazil, stray dogs and cats are important reservoirs in urban areas, whereas in rural areas pigs are the most import species [30,31]. Pigs were also identified as the major reservoir *of T. penetrans* in Nigeria and in Uganda [15,25]. However, pigs were not kept in any of the households in the study area, because a considerable part of the population is Muslim. Actually, being Muslim was identified as a significant protective factor in the bivariate analysis (Table 5), which may be explained by the fact that Muslims wash their feet several times a day before entering the mosque for prayer.

Other risk factors which remained significant after multivariate regression analysis were the limited access to water (water only available from muddy pools), frequency of washing as well as bathing without soap. A similar finding was made in a resource-poor community in Northeast Brazil [14]. It is tempting to speculate that these risk factors are correlated to the reproductive biology of *T. penetrans*. Female sand fleas are fertilized by males exploring the skin only after females are embedded in the epidermis and have started neosomy [32]. There is circumstantial evidence that males are attracted by odor emitted from the faecal material released by females in regular intervals [12,13]. The faecal material spreads into dermal papillae around the lesion, and since it is very sticky, it needs soap to be washed off. Hence, when soap is not used or unavailability of water prevents any washing at all, more male sand fleas should be attracted to the skin and, hence, more females will be fertilized. Over time, this will lead to a higher intensity of infection.

It has previously been reported that within endemic areas, tungiasis is heterogeneously distributed [2]. This was confirmed in this study: where prevalence varied between villages from 7.8% to 64.7% in the five study villages in Malanga Sub-location, all situated within 4 km of each other and from 13.4% to 35.5% in the three study villages in Kakuyuni Sub-location, within 2 km of each other. Whether the heterogeneity is determined by differences in the predominant type of exposure within a community, such as intra-domiciliary versus peri-domestic could not be clarified in this study.

We found very high Population Attributable Fractions for biologically very plausible variables. Trickling of sand and dust from mud walls creates ideal conditions for the off-host life cycle of sand fleas in cracks of the floor. Building walls of stone or cement would reduce the prevalence of tungiasis by 64 percent. Similar, promoting better hygiene, particularly washing with soap, would reduce the prevalence of tungiasis in the community by 17 and 20%, respectively.

We realize that this study has several limitations. First, there is an overrepresentation of adult females in the study group. The study was conducted during the day on all days of the week, including Saturday and Sunday, in order to encounter school children on the compound. However, since the majority of adult males in our study population worked as farmers and returned only after sunset we could not examine them. Extending our working periods towards the evening was not possible due to insufficient lighting and safety concerns. The distances between the households in Malanga and our time constraints, also meant that there were fewer households included in the study from this area than from Kakuyuni. Ecologically the two areas are quite different.

Taken together, many factors which—by one way or another—are linked to poverty were identified as important risk factors in the bivariate and/or multivariate regression analysis, such as poor construction characteristics of the house, absence of a ventilated pit latrine, no access to drinking water on the compound, a single sleeping room for children and adults, absence of beds and mattresses, unavailability of soap for body wash, an asset score below 5 points and a low level of education among adults. Thus, as seen elsewhere in the world, tungiasis in rural Kenya is a poverty-associated disease in which the poorest of the poor bear the highest burden of disease, but that it can be controlled with simple housing improvements, improved access to water and hygiene practices.

Supporting information

S1 Appendix. Household informed consent.
(DOCX)

S2 Appendix. Database. Prevalence of tungiasis in 5 schools in Kilifi County.
(DOCX)

S3 Appendix. Domestic husbandry practices.
(DOCX)

S4 Appendix. STROBE checklist.
(DOC)

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PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Prevalence, intensity and risk factors of tungiasis in Kilifi County, Kenya II: Results from a school-based observational study

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Abstract

Introduction

Awareness of the public health importance of tungiasis has been growing in East Africa in recent years, but data on epidemiological characteristics necessary for the planning and implementation of control measures do not exist. The work presented here was part of a larger cross-sectional study on the epidemiology of tungiasis in coastal Kenya and aims at identifying risk factors of tungiasis and severe disease in school children.

Methods

A total of 1,829 students of all age groups from five schools and 56 classes were clinically examined for tungiasis on their feet based on standardized procedures and observations made about the school infrastructure. To investigate the impact of school holidays, observations were repeated after school holidays in a subset of children in one school. In an embedded case-control study, structured interviews were conducted with 707 students in the five schools to investigate associations between tungiasis and household infrastructure, behaviour and socio-economic status.

Results

The overall prevalence of tungiasis was 48%; children below the age of 15 years were the most affected, and boys were twice as likely as girls to be infected. The highest risk of disease was associated with the socio-economic circumstances of the individual student at home. The study indicated that mild to moderate tungiasis could be reduced by a third, and severe tungiasis by over half, if sleeping places of children had hardened floors, whilst approximately a seventh of the cases could be prevented by sealing classroom floors in schools, and another fifth by using soap for daily feet washing.

factor survey_DATA_Interviews https://doi.org/10.7910/DVN/VF7R2W.

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Competing interests: The authors have declared that no competing interests exist.

Conclusion

There is a clear role for public health workers to expand the WASH policy to include washing of feet with soap in school-aged children to fight tungiasis and to raise awareness of the importance of sealed floors.

Author summary

Tungiasis is a neglected tropical skin disease caused by penetrated sand fleas, the adult female of which burrows into the skin of the feet. The parasite rapidly expands its body size by a factor of 2000. The growth causes immense itching, inflammation, pain and debilitation. The current lack of good treatment methods means people attempt to remove the fleas themselves with non-sterile instruments causing more damage. Control efforts focus on prevention but there is little data to guide this in East Africa. The current study reinforces our previously published results on the household level from the same communities, indicating that prevention needs to focus on hardening the floors of resource-poor families and integrating daily foot washing with soap into water, hygiene and sanitation programs.

Introduction

Sand flea disease (tungiasis) is a highly neglected parasitic skin disease which inflicts pain and suffering on millions of impoverished people in South America, the Caribbean and sub-Saharan Africa. Research on tungiasis is scant and most of the publications originate from South America [1] [2],very little work has been done in sub-Saharan Africa. This is partly because even though the disease bears all the hallmarks of a Neglected Tropical Disease [1] it was until very recently [3] not included in the World Health Organisation's list of Neglected Tropical Diseases. This made it difficult for funding organisations to invest research funds into determining the disease ecology and consequently the development of urgently needed treatment and prevention tools. Most research currently undertaken on tungiasis is small-scale, supported by national and international non-governmental organizations and well-wishers, reinforced by community-based self-help groups and is hence highly resource-constrained [2].

The development of the juvenile stages of the sand flea *Tunga penetrans*, is similar to that of other Siphonaptera; they live off the host but depend during their development on loose, sandy soil [4, 5]. In contrast to other flea species, the adult female sand flea becomes permanently parasitic on its host, where it burrows into the skin and undergoes a dramatic growth, increasing its volume about 2000-fold within eight days [6]. Tungiasis affects mostly the feet and is associated with a pattern of debilitating morbidity [6]. Itching, pain, swelling, deep fissures, ulcers and abscess formation are symptoms of an acute inflammatory response to embedded fleas and bacterial superinfections of the lesions. Chronic infections result in chronic pain, disability, disfigurement and mutilation of the feet [6, 7, 8]. Children with tungiasis are often ridiculed by their peers and it has been shown that physical incapacity, mental strain and distress reduce quality of life [9].

Awareness of the public health importance of tungiasis has been growing in East Africa in recent years [10], but data on epidemiological characteristics, necessary for the planning and implementation of a control program, do not exist. The work presented here was part of a larger observational study performed in disease endemic areas in coastal Kenya and included simultaneously implemented cross-sectional household-based risk factor surveys recently published [11] and school-based surveys presented here. To the best of our knowledge, combined, the two studies provide the most comprehensive risk factor study to date on tungiasis for Sub-Saharan Africa.

Methods

The aim of the school-based study was to complement the household-based study to investigate prevalence and risk factors for tungiasis and whether targeting school-going children for treatment and prevention might be a viable option. The specific objectives included: 1) determine the prevalence of tungiasis in selected rural schools in Malindi sub-county, 2) whether there are specific school factors associated with disease, 3) whether school or home present the greater risk and 4) if similar or different risk factors associated with the disease might be identified through a school-based survey.

Study area and population

The study was performed in Malindi Sub-county, Kilifi County, eastern Kenya, where tungiasis is endemic and previous reports indicated disease prevalence in villages to range from 8% to 65% [11]. Malindi Sub-county is divided into two ecological zones: Kakuyuni Sub-location, a densely populated area in the coastal strip with tropical climate, and Malanga Sub-location, a less densely populated area inland with a much drier climate. Most rural homesteads in these areas consist of several mud-walled houses with a palm thatch roof and sandy floor. Domestic animals such as goats, cats, dogs and chickens walk freely on the compounds. Subsistence farming is the only activity practiced by most of the population to sustain their livelihood.

The cross-sectional study was implemented between August 5 and October 3, 2014 in five primary schools; two schools in Kakuyuni Sub-location (labelled as KS1 and KS2), and three schools in Malanga Sub-location (labelled as MS1, MS2, MS3). Schools were a minimum of 2 km apart with distinct catchment areas from where children originated. All except MS3 were public schools. The schools were purposely selected based on recommendation from the county Public Health Department as schools that were affected by tungiasis and no interventions had previously taken place in the catchment areas of these schools. The schools were located in the same communities as the household study. For the risk factor study a case: control design was used with a 1:1 ratio. The sample size calculation to yield results with 95% confidence limits, 80% power, an assumed prevalence of exposure of 40% among controls and least extreme odds ratio to be detected of 1.5, indicated the need for a sample of 776 students (388 cases, 388 controls). To allow for incomplete data sets and be able to adjust for confounders we increased this by 20%, aiming to interview 930 students (465 cases, 465 controls).

All schools were single-storey buildings and all were divided into several classrooms. MS2 had some classrooms of concrete and some of mud while all in MS3 were mud walls. The floor quality of the classrooms ranged from smooth cement surfaces to loose sand/soil (Fig 1). All schools had access to water and according to the information from the class teachers, classroom floors were swept daily by the students. For all classes, the classroom size, the number of students per class, and the type of classroom floor, walls and roof were recorded.

Clinical examination

All female and male students of all age groups, for whom informed consent and assent was given, were clinically examined for tungiasis, class by class. Prior to the clinical examination, the feet of the students were carefully washed with soap in a basin. Each individual was then examined for tungiasis based on a standardized procedure [11], focussing on their feet and

Fig 1. Examples of school classroom floors. (A) Natural sand/soil (MS2). (B) Cracked concrete (MS1). (C) Smooth concrete (MS1).

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hands since a high number of lesions at the feet frequently coincide with the presence of ectopic lesions at the hands [12]. Patients were also asked whether they had tungiasis lesions in other regions of the body. Lesions were counted and staged according to the Fortaleza classification [6] as stage I: penetrating sand flea; stage II: brownish/black dot with a diameter of 1–2 mm surrounded or not by an erythema; stage III: circular yellow-white watch glass-like patch with a diameter of 3–10 mm and with a central black dot; stage IV: brownish-black crust with or without surrounding necrosis. Stage I to III are viable sand fleas. In stage IV the parasite is dying or already dead (non-viable). Lesions manipulated with a sharp instrument (by the patient or their caregiver) with the intention to remove the embedded parasite were documented as manipulated lesions. Based on the number of lesions present, the intensity of tungiasis was classified as light (1–5 lesions), moderate (6–30 lesions) or severe (>30 lesions) [13]. For every patient, the age, sex, and class were recorded.

To investigate potential changes in the presentation of tungiasis in students after school holidays we aimed to repeat the clinical examinations in as many students as possible in KS1 who had been originally examined in the week immediately before the 4-week August holiday. Only 248 of the original group of students examined could be traced in the first week after the holiday.

Structured interviews

Within each school a subset of students was selected for interviews. In KS1 and MS1, all tungiasis cases over the age of 4 years and the following uninfected student (as an age-matched control) were interviewed. In the remaining schools, only the first half of the cases (in chronological order of their identification) and the following uninfected student, were interviewed due to time constraints. It was not possible to recruit equal numbers of controls for interviews in MS2 and MS3 because the majority of students had tungiasis. Structured interviews were conducted using a pre-tested questionnaire in Giriama or Swahili language, including questions about the physical structure of the house in which children slept (house walls, roof and floor), water sources and access at home, hygiene habits (washing frequency, soap use, toilet facility at home), livestock and companion animals kept in homestead and walking time to school. Furthermore, observations were recorded about the condition of the students' school uniforms and the type of shoes worn if any.

Statistical analysis

Generalized Estimating Equations were used to analyse potential associations between the prevalence of tungiasis or the number of lesions (of different stages) and multiple variables recorded during interviews and observations. Prevalence data were modelled using binomial probability distributions with logit link functions fitted, count data were modelled using negative binomial probability distributions with log link functions fitted. Depending on the analysis the unique school ID, the unique class ID or the unique student ID were included as repeated measure and an exchangeable correlation matrix assumed. In the final multivariable risk factor analyses only factors found significant when tested individually in a univariate analysis were included as predictors. Interactions were explored for variable combinations that were plausible to be potentially interacting. In the final model, only significant interactions were included. All reported mean proportions or mean counts and their 95% confidence intervals (CIs) were estimated as the exponentials of the parameter estimates for models with no intercept included. Frequency counts were compared using the Pearson Chi-Square test. The analyses were done with R statistical software version 2.14.2 [14]. Population Attributable Fractions (PAF) were calculated, representing the fraction of cases which would not have occurred if an exposure had been avoided, assuming the exposure is casual and the other risk factors in the population remain unchanged [15]. PAFs are the percent exposed among cases multiplied by the attributable risk (AR). The AR is the risk of tungiasis in the exposed due to the exposure and is calculated as (odds ratio (OR) −1)/OR.

Ethical considerations

The study was approved by the Ethics Review Committee at Pwani University, Kilifi County, Kenya; approval number ERC/PhD/010/2014. During the study preparation phase contact was made with the County and District leadership in the Ministry of Health and the Ministry of Education, the Zonal Education Officer and the Community Health Officers to obtain their approvals and support for the study. Meetings were held with Community Health Workers (CHWs) in each sub-location, training on tungiasis provided and the aims and procedures of the study explained, emphasizing that participation was completely voluntary, and subjects had the opportunity to withdraw from the study at any point in the study. Head Teachers were visited and provided with an information sheet. The information was read out at a parents' meeting prior to the study, explaining the procedure and voluntary nature of participation, and asking for consent. The Head Teacher signed the consent form (S1 Annex) on behalf of the parents and school. Data were collected with the help of Community Health Volunteers of the respective Community Health Unit. All data analyses were conducted anonymously.

All students with tungiasis were treated after the survey by the Community Health Workers according to standard practice in Kilifi County [10]. For those with secondary bacterial infection and other illnesses requiring treatment, a referral form was prepared by a Community Health Worker, and patients were referred to the nearest Health Facility.

Results

A total of 1,829 students from 56 classes in the 5 schools were examined, about 70% of the students enrolled in the schools (total 2,622) based on school records. Of these, 923 students were interviewed, just short of the calculated sample size of 930, but only 707 had fully completed the interview and were included in the data analysis; 398 were cases and 309 were controls (Fig 2).

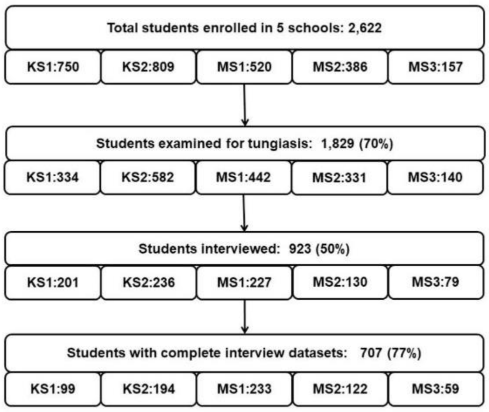

Fig 2. Flow chart of study population.

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Prevalence of tungiasis and intensity of infection

Of the examined 1,829 primary school students 48% were boys and 52% were girls; 31% of the students were 2–9 years old, 52% 10–14 years old and 17% were 15–21 years old. Of the 870 (48% of 1,829) students with tungiasis, 58% had mild infections (1–5 lesions), 31% moderate (6–30 lesions) and 11% severe infections (>30 lesions;). The majority of all cases were males aged 10–14 years (28.4% of cases, Fig 3) and also had the highest percent of moderate and severe cases. The student population size examined ranged from 140 to 582 between schools and the prevalence of tungiasis varied significantly between the five schools ranging from 31% to 83% (Table 1).

The physical school environment was considered a potential risk factor for tungiasis either directly providing a conducive environment for the off-host host stages to develop and adult sand fleas to find a host or indirectly as a proxy measure for the socio-economic circumstances affecting the community from which the children were drawn to the respective schools

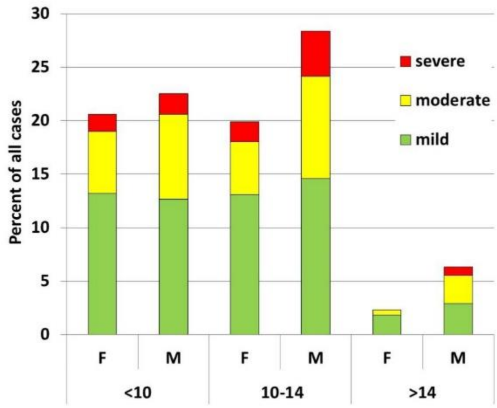

Fig 3. Severity of tungiasis by age group and sex. n = 870 cases; viable, non-viable and manipulated lesions combined. Mild < 6 fleas, moderate = 6–30 fleas and severe >30 fleas.

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Table 1. Multivariable analysis for tungiasis prevalence in the five schools surveyed.

Parameter	Total examined (n)	Modelled mean tungiasis prevalence (%)	95% Confidence Interval (CI)		Odds Ratio (OR)	95% Confidence Interval (CI)		*p*
			Lower	Upper		Lower	Upper	
School								
MS3	140	83	75	88	2.54	0.85	7.57	0.094
MS2	331	75	68	82	1.88	0.82	4.32	0.139
MS1	442	34	29	38	0.77	0.48	1.24	0.279
KS2	582	51	37	65	2.35	0.82	6.76	0.112
KS1	334	31	26	36	1.00			
Classroom floor								
natural sand/soil	268	80	74	85	3.00	1.15	7.79	0.024
cracked concrete	725	49	43	55	0.51	0.30	0.87	0.014
smooth concrete	836	46	38	55	1.00			
Interaction school * classroom floor								
MS3*natural sand/soil	140	83	75	88	1.00			
MS2*natural sand/soil	128	78	67	86	1.00			
MS2*cracked concrete	69	87	77	94	11.54	3.30	40.37	<0.001
MS2*smooth concrete	134	54	36	72	1.00			
MS1*cracked concrete	96	35	30	40	2.16	1.13	4.13	0.020
MS1*smooth concrete	346	33	26	40	1.00			
KS2*cracked concrete	370	43	31	56	0.99	0.30	3.32	0.987
KS2*smooth concrete	212	60	35	81	1.00			
KS1*cracked concrete	190	24	18	32	1.00			
KS1*smooth concrete	144	39	31	47	1.00			
Sex								
Male	874	65	60	71	2.37	1.89	2.97	<0.001
Female	955	44	40	49	1.00			
Age								
2–9 years	571	60	54	66	1.57	1.04	2.36	0.032
10–14 years	942	56	50	62	1.35	1.07	1.69	0.011
15–21 years	316	49	41	57	1.00			

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(children from poor background might only be able to afford sending children to a school with very basic school environment). Size, materials of the floors, walls and roofs were recorded for every classroom from which children were examined during the surveys. The majority (70%) of the students were taught in classrooms between 40–70 m^2 while 22% were taught in classrooms larger than 70 m^2 and only 8% in classrooms smaller than 40 m^2. Classroom size was not significantly associated with tungiasis prevalence in a univariate analysis, and neither was the number of children per m^2 in a classroom, which ranged from 0.4 to 2.0.

Most classroom floors were made of concrete; 46% of all screened students were taught in a room with a good quality concrete floor and 40% in a classroom with cracked concrete floor. Concrete floors were always associated with concrete walls and iron sheet roofs. Only 14% of the surveyed students studied in classrooms with a natural sand/soil floor. These classrooms also had mud walls and thatched roofs (Fig 1).

The differences in tungiasis prevalence between schools were confounded by the physical classroom environment as revealed by the multivariable analysis (Table 1). The floor type of the classroom was an important risk factor for finding a tungiasis case, the degree of risk per floor type, however, was dependent on the school, as shown by the significant interaction between floor type and school. Natural sand or soil floor of a classroom was an independent risk factor, increasing the probability of finding a tungiasis case 3-fold as compared to finding a case among students that were taught in a classroom with a well-kept, smooth concrete floor. Classrooms with natural sand/soil floors were only present in MS2 and MS3, the two schools with the highest tungiasis prevalence. Whether a cracked concrete floor represented a risk for finding a tungiasis case depended significantly on the school. The impact of the interactions can be calculated by multiplication of the odds ratios [16]. This means a cracked concrete floor was only a factor significantly associated with increased disease risk in MS2 (OR 11.54 x OR 0.51 = OR 5.89), where classrooms with sand/soil and concrete floors coexisted but not in MS1 (OR 2.16 x OR 0.51 = OR 1.10; Table 1). Consequently, floor type was not an explanatory variable for tungiasis prevalence in KS1, KS2 and MS1, where tungiasis prevalence ranged between 31% and 51% (Table 1).

Both age and sex were significantly, and independently associated with tungiasis. Children below the age of 15 years were 1.4–1.6 times more likely to be diagnosed with tungiasis than older students and boys more than 2 times more likely than girls (Table 1).

No specific school-based risk factors were significantly associated with severe tungiasis, when the multivariable analysis was repeated with severe manifestation as the dependent variable.

Comparison of tungiasis prevalence and numbers of viable, non-viable and manipulated lesions before and after school holidays

Anecdotal information provided by the teachers suggested that children usually return to school with a higher tungiasis burden after school holidays. To investigate this, we compared the tungiasis prevalence and infection status immediately before and after the one-month August school holiday in the 248 students who were able to be traced in the first week after the holiday in KS1 (Tables 2 and 3). This sub-group comprised 41% boys, 59% girls, with 23% <10 years old, 55% 10–14 years old and 22% 15–20 years old.

Sex and age were identified, similar to the analysis on the larger data set, as independent risk factors for tungiasis before and after the school holidays, with boys and younger age groups more likely to be found with the disease than girls and older age groups (Table 2). There was no significant interaction between sex, age and survey time. The probability of finding a tungiasis case after the school holidays was 1.7 times higher than before the holidays,

Table 2. Multivariable analysis to investigate the association between school holidays and tungiasis prevalence in KS1.

Parameter	Total examined (n)	Modelled mean tungiasis prevalence (%)	95% Confidence Interval (CI)		Odds Ratio (OR)	95% Confidence Interval (CI)		*p*
			Lower	Upper		Lower	Upper	
Sex								
Male	202	50	40	60	3.07	1.89	5.01	<0.001
Female	294	26	19	33	1.00			
Age								
2–9 years	116	48	37	59	2.94	1.37	6.29	0.006
10–14 years	272	38	30	45	1.70	0.86	3.35	0.126
15–21 years	108	27	16	41	1.00			
Survey								
after holidays	248	44	36	51	1.71	1.31	2.23	<0.001
before holidays	248	31	25	38	1.00			

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Table 3. Multivariable analyses investigating the risk of finding viable, non-viable and manipulated lesions after school holidays in KS1 as compared to the baseline survey.

Parameter	Total tungiasis cases analysed (n)	Modelled mean number of lesions*	95% Confidence Interval (CI)		Rate Ratio (RR)	95% Confidence Interval (CI)		*p*
			Lower	Upper		Lower	Upper	
(A) Viable lesions								
Sex								
Male	105	1.53	0.93	2.51	0.77	0.34	1.74	0.531
Female	79	1.32	0.79	2.23	1.00			
Age								
2–9 years	54	0.88	0.44	1.74	0.68	0.21	2.25	0.528
10–14 years	104	1.79	1.13	3.83	1.13	0.40	3.21	0.819
15–21 years	26	1.83	0.86	3.89	1.00			
Survey								
after holidays	106	0.80	0.50	1.29	0.30	0.10	0.84	0.023
before holidays	78	2.52	1.61	3.93	1.00			
Sex*Survey								
male*after holidays	58	1.06	0.60	1.86	2.24	0.86	5.84	0.098
male*before holidays	47	2.21	1.21	4.03	1.00			
female years*after holidays	48	0.61	0.30	1.23	1.00			
female*before holidays	31	2.87	1.56	5.27	1.00			
Age*Survey								
2–9 years*after holidays	32	0.41	0.15	1.10	0.49	0.12	2.05	0.331
2–9 years*before holidays	22	1.87	0.81	4.33	1.00			
10–14 years*after holidays	59	1.03	0.59	1.79	0.75	0.31	1.82	0.519
10–14 years*before holidays	45	3.10	1.79	5.37	1.00			
15–21 years *after holidays	15	1.22	0.54	2.76	1.00			
15–21 years*before holidays	11	2.75	1.15	6.50	1.00			
(B) Non-viable lesions								
Sex								
Male	105	4.03	2.87	5.68	1.18	0.72	1.94	0.519
Female	79	3.42	2.29	5.12	1.00			
Age								
2–9 years	54	3.30	1.94	5.61	2.62	0.83	8.29	0.101
10–14 years	104	5.33	3.97	7.17	4.46	1.59	12.46	0.004
15–21 years	26	2.92	1.53	5.23	1.00			
Survey								
after holidays	106	3.06	2.19	4.27	2.14	0.63	7.34	0.225
before holidays	78	4.52	3.02	6.75	1.00			
Age*Survey								
2–9 years*after holidays	32	2.09	1.19	3.67	0.19	0.05	0.72	0.015
2–9 years*before holidays	22	5.22	2.79	9.74	1.00			
10–14 years*after holidays	59	3.21	2.17	4.74	0.17	0.04	0.66	0.01
10–14 years*before holidays	45	8.87	5.76	13.68	1.00			
15–21 years *after holidays	15	4.27	2.06	8.85	1.00			
15–21 years*before holidays	11	1.99	0.77	5.16	1.00			
(C) Manipulated lesions								
Sex								
Male	105	9.18	6.87	12.26	2.61	1.44	4.74	0.002
Female	79	5.40	4.04	7.21	1.00			

(*Continued*)

Table 3. (Continued)

Parameter	Total tungiasis cases analysed (n)	Modelled mean number of lesions*	95% Confidence Interval (CI)		Rate Ratio (RR)	95% Confidence Interval (CI)		p
			Lower	Upper		Lower	Upper	
Age								
2–9 years	54	6.52	4.80	8.85	0.90	0.38	2.11	0.807
10–14 years	104	7.30	5.54	9.62	0.67	0.29	1.56	0.357
15–21 years	26	7.33	4.41	12.17	1.00			
Survey								
after holidays	106	10.02	8.23	12.20	2.41	1.19	4.90	0.015
before holidays	78	4.94	3.57	6.84	1.00			
Sex*Survey								
male*after holidays	58	10.55	7.86	14.16	0.42	0.21	0.85	0.016
male*before holidays	47	7.98	5.35	11.91	1.00			
female years*after holidays	48	9.52	7.24	12.53	1.00			
female*before holidays	31	3.06	1.89	4.94	1.00			
Age*Survey								
2–9 years*after holidays	32	8.09	5.56	11.78	0.98	0.44	2.17	0.961
2–9 years*before holidays	22	5.25	3.36	8.21	1.00			
10–14 years*after holidays	59	13.55	10.15	18.08	2.19	1.08	4.45	0.03
10–14 years*before holidays	45	3.94	2.55	6.08	1.00			
15–21 years *after holidays	15	9.19	6.36	13.27	1.00			
15–21 years*before holidays	11	5.84	2.81	12.13	1.00			

*modelled for cases (students with any lesions) only

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with a mean prevalence in students of 31% (95% CI 25–38%) before and 44% (95% CI 36–51) after the holidays (Table 2).

Taking a closer look at the number and developmental stage of the embedded sand fleas (Table 3), we observed that the number of viable lesions in students with tungiasis had significantly decreased (RR 0.30 (95% CI 0.10–0.84), p = 0.023) after the holidays from a mean number of 2.52 (95% CI 1.61–3.93) viable lesions before to 0.80 (95% CI 0.50–1.29) after the holidays, irrespective of sex and age. The number of non-viable lesions was generally highest in students with tungiasis between 10–14 year of age irrespective of sex and survey round, however significantly decreased (RR 0.17 (95% CI 0.04–0.66), p = 0.010) after the holidays from a mean of 8.87 to a mean of 3.21 (Table 3). A proportionally similar decrease in non-viable lesions was also seen in the younger age group of 2–9 years old students but not in the older students as shown by the significant interactions between age and survey round (Table 3). On the contrary, the number of manipulated lesions increased significantly after the school holidays. Significant interactions in the analysis (Table 3) highlighted a proportionally higher increase in manipulated lesions in girls from 3.06 (95% CI 1.84–4.94) before to 9.52 (95% CI 7.24–12.53) after holidays, than in boys, even though boys had overall a larger number of manipulated lesions (mean before holidays 7.98 (95% CI 5.35–11.91); after holidays 10.55 (95% CI 7.86–14.16)). There was also a proportionally higher increase in the number of manipulated lesions in the 10-14-year-old students than in the other age groups (Table 3).

Behavioural and socio-economic tungiasis risk factors identified from structured student interviews and observations

Most of the characteristics assessed by observation and interview, for each of the 707 students interviewed, showed considerable heterogeneity between schools, except for sex and ownership of dogs and chickens (Table 4).

The significant between-group variations for schools was taken into consideration by including the school as a random factor in the subsequent multivariable analyses of the interview data (Table 5). Since tungiasis cases and healthy controls were matched by age at the enrolment stage, age was not a factor significantly associated with tungiasis as an outcome in the analysis of the interview data and hence not included in the multivariable analysis. Expectedly, sex was similarly associated with tungiasis risk in the interview data, with boys being >2 times more likely to be found with tungiasis than girls. The condition of the school uniform was not independently associated with tungiasis, but an interaction existed with sex. The chance of finding tungiasis was significantly higher (OR 4.30 (95% CI 1.47–12.60), p = 0.008) in boys with torn school uniforms than in boys with better uniforms or in girls with torn uniforms (Table 5).

Similarly, the absence or presence of open or closed shoes was not by itself a risk factor for tungiasis. When a child was however found not wearing shoes and had a badly torn school uniform it was highly likely (OR 5.32 (95% CI 3.22–8.79), p<0.001) to find tungiasis (Table 5). The time a child took to walk to school was not significantly associated with presence of tungiasis in the multivariable analysis. Whilst the building material of the students' homes floors, walls, and roofs were all associated with tungiasis in a univariate analysis only the home's floor was an independent risk factor in the multivariable analysis. A student from a home with a natural sand or mud floor indoors was nearly twice as likely to be diagnosed with tungiasis, than a student from a home with a concrete floor in the house (Table 5). Most of the students had access to piped water or a well either on their compound or shared in the village. Nevertheless, students coming from a home where water was fetched from a community tap or well were 1.6 times more likely to have tungiasis than those students that had tap water on their compound at home. The time it takes for the family to fetch water was not associated with the disease outcome. Whilst the frequency of washing feet was not associated with the presence of tungiasis, the use of soap strongly was. Students that responded never to wash their feet with soap were over 6 times more likely (95% CI = 3.2–12.6, p<0.001) to have tungiasis and students that responded to only sometimes wash they feet with soap were 1.6 times more likely (95% CI 1.50–1.76, p<0.001) to have tungiasis than those students always washing with soap (Table 5). Although washing frequency responses were not significantly associated with tungiasis, not answering this question was (OR 6.01 (95% CI = 3.64–9.92), p<0.001). Neither the type of toilet at home, nor the presence of a dog on the compound, were significantly associated with disease outcome when the analysis was adjusted for all other variables.

In an attempt to better understand what drives severe infection (>30 embedded lesions) we performed a multivariable analysis for severe disease as the outcome (n = 71, 18% of all cases N = 398), comparing the characteristics of these severe cases with mild to moderate cases (1–30 lesions, n = 327). Sex, condition of clothing, shoe-wearing and frequency of soap use were not significantly associated with disease severity. Of all tungiasis cases, severe infections were more likely to be found in the younger age groups (Table 6), in children having a natural sand/mud floor indoors at home than those that have a stone/cement floor at home, using a water source other than a private or community tap or well, and washing their feet less than once a day. Of all children with tungiasis, those that reported their family did not own at least one chicken had a significantly higher risk of heavy infection than children who reported they kept

Table 4. Frequency of individual and household characteristics identified by interview and observation per school (*p = Pearson Chi-Square).

Explanatory variables	Variable categories	Percent (%) of all students interviewed per school					Total n = 707	p*
		KS1	KS2	MS1	MS2	MS3		
		n = 99	n = 194	n = 233	n = 122	n = 59		
Sex	female	44	44	49	38	54	46	0.212
	male	56	56	51	62	46	54	
Age group	2–9 years	3	26	16	30	68	24	<0.001
	10–14 years	70	60	69	51	32	60	
	15–21 years	27	15	15	19	0	16	
Shoes worn to school	closed shoes	14	7	10	6	3	9	<0.001
	open shoes	61	56	54	31	36	50	
	no shoes	25	37	36	63	61	41	
Walking time to school	less 30 minutes	54	54	63	63	51	58	<0.001
	more 30 minutes	35	34	37	36	29	35	
	no answer	11	12	0	1	20	7	
Condition of uniform	good	7	14	58	69	70	42	<0.001
	moderate	70	73	40	27	31	50	
	torn	23	13	1	4	0	8	
Material of home floor	stone/cement	25	15	10	5	12	13	<0.001
	smeared mud	19	23	37	13	17	25	
	sand	56	62	53	83	71	62	
Material of home walls	stone/cement	25	17	5	4	0	11	<0.001
	smeared mud	74	83	94	95	100	89	
	palm leaves	1	1	1	1	0	1	
Material of home roof	thatched	61	51	54	64	44	55	0.042
	corrugated iron sheets	39	49	46	36	56	45	
Source of water at home	tap on compound	34	39	7	8	5	20	<0.001
	shared community tap/ well	57	62	93	92	93	79	
	other	9	0	0	0	2	1	
Time to fetch water at home	less than 15 minutes	80	82	72	58	58	72	<0.001
	more than 15 minutes	12	8	28	41	19	22	
	no answer	8	9	0	2	24	6	
Frequency of washing feet per day	twice a day	70	70	83	74	70	75	<0.001
	once a day	18	25	16	13	5	17	
	less often	6	5	2	0	0	3	
	no answer	6	1	0	13	25	5	
Frequency of using soap for washing feet	always	66	56	25	16	24	38	<0.001
	sometimes	24	39	72	68	49	53	
	never	9	4	3	3	2	4	
	no answer	1	2	0	14	25	5	
Type of toilet at home	WC	14	16	8	6	10	11	<0.001
	latrine	36	56	57	53	54	53	
	bush	50	27	36	29	31	34	
	no answer	0	1	0	12	5	3	
Household owns dog	yes	34	24	32	30	27	30	0.352
Household owns chicken	yes	94	97	96	94	95	95	0.745

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Table 5. Multivariable analysis exploring the association of observational and interview data with tungiasis outcome.

Explanatory variables	Total interviewed (n)	Modelled mean tungiasis prevalence (%)	95% Confidence Interval (CI)		Odds Ratio (OR)	95% Confidence Interval (CI)		P
			Lower	Upper		Lower	Upper	
Sex								
male	381	79	66	88	2.55	1.25	5.20	0.010
female	326	47	31	64	1.00			
Condition of uniform								
torn	55	67	44	84	0.43	0.12	1.55	0.197
moderate	356	68	51	81	1.54	0.83	2.85	0.172
good	296	59	47	71	1.00			
Sex*condition of uniform								
male*torn	36	86	72	95	4.30	1.47	12.60	0.008
male*moderate	215	77	61	88	0.99	0.44	2.25	0.985
male*good	130	70	56	81	1.00			
female*torn	19	38	18	63	1.00			
female*moderate	141	57	41	72	1.00			
female*good	166	48	33	63	1.00			
Shoes worn during survey (observed)								
none	293	78	60	89	1.61	0.67	3.87	0.289
open	353	61	46	74	1.80	0.70	4.63	0.223
closed	61	53	35	71	1.00			
Interaction clothes condition*shoes worn								
torn*none	25	89	70	96	5.32	3.22	8.79	<0.001
torn*open	26	53	38	68	0.69	0.15	3.10	0.629
torn*closed	4	48	19	78	1.00			
moderate*none	152	77	57	89	1.31	0.78	2.20	0.301
moderate*open	169	64	49	78	0.64	0.29	1.41	0.270
moderate*closed	35	61	41	78	1.00			
good*none	116	62	52	72	1.00			
good*open	158	65	49	78	1.00			
good*closed	22	51	30	71	1.00			
Walking time to school								
no answer	47	66	46	82	1.08	0.79	1.49	0.620
>30 minutes	247	64	50	76	0.98	0.69	1.39	0.918
<30 minutes	413	64	49	77	1.00			
Material of floor at home								
sand	439	70	56	82	1.88	1.64	2.15	<0.001
smeared mud	178	68	50	81	1.65	1.26	2.15	<0.001
stone/concrete	90	56	40	71	1.00			
Material of wall at home								
matts from plam leaves	5	59	31	82	0.61	0.22	1.69	0.342
mud	628	64	53	74	0.75	0.50	1.11	0.147
stone/concrete	74	71	55	83	1.00			
Material of roof at home								
thached	389	67	50	80	1.17	0.85	1.60	0.332
corrugated iron sheet	318	63	47	77	1.00			
Source of water at home								
other	10	52	25	77	0.56	0.25	1.27	0.165

(Continued)

Table 5. (Continued)

Explanatory variables	Total interviewed (n)	Modelled mean tungiasis prevalence (%)	95% Confidence Interval (CI)		Odds Ratio (OR)	95% Confidence Interval (CI)		*P*
			Lower	Upper		Lower	Upper	
community tap/well	559	76	65	84	1.63	1.44	1.85	<0.001
tap on compound	138	65	55	74	1.00			
Time to fetch water at home								
no answer	43	68	57	76	1.21	0.64	2.30	0.564
>15 minutes	153	63	43	80	0.99	0.64	1.52	0.959
<15 minutes	511	63	42	81	1.00			
Number of times feet washed								
no answer	40	87	80	91	6.01	3.64	9.92	<0.001
less than daily	19	55	36	72	1.12	0.62	2.02	0.705
once a day	121	57	37	76	1.24	0.68	2.28	0.480
twice a day	527	52	32	72	1.00			
Frequency of soap use								
no answer	38	37	25	50	0.47	0.25	0.89	0.020
never	28	89	70	96	6.33	3.17	12.64	<0.001
sometimes	377	67	52	79	1.62	1.50	1.76	<0.001
always	264	55	41	69	1.00			
Type of toilet at home								
no answer	20	76	28	96	2.11	0.18	25.17	0.555
bush	237	60	48	71	1.02	0.57	1.82	0.957
latrine	374	61	48	73	1.05	0.71	1.56	0.812
water closet	76	60	41	77	1.00			
Dog at home								
present	209	70	52	83	1.63	0.93	2.85	0.085
absent	498	59	42	74	1.00			
Student's classroom floor								
natural sand/soil	112	78	64	88	3.08	2.39	3.97	<0.001
cracked concrete	291	59	44	73	1.24	1.12	1.37	<0.001
smooth concrete	304	54	37	70	1.00			

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chicken (Table 6). Amongst all children with tungiasis, school floor characteristics were not a predictor for heavy infection.

Population attributable fractions (PAF)

For those factors which were significant risks for tungiasis or a high intensity of infection, and are amenable to being changed, the PAF were calculated. The PAF is the percent reduction in prevalence that would occur if exposure to the risk factor were removed. The highest PAF for both, any infection and severe infection was found to be having a home floor of sand or smeared mud (30.7% and 54.4% respectively, Table 7). Only using soap sometimes when washing had a PAF of 21.5%, and a classroom floor of sand had a PAF of 14.3% for any type of infection.

Discussion

Our study confirmed that the prevalence of tungiasis is extremely heterogeneous, varying from school to school and community to community even though they are only a few

Table 6. Multivariable analysis exploring the association of observational and interview data with severe tungiasis amongst all tungiasis cases.

Parameter	Total cases interviewed (n)	Modelled mean percentage (%) of severe tungiasis cases*	95% Confidence Interval (CI)		Odds Ratio (OR)	95% Confidence Interval (CI)		*p*
			Lower	Upper		Lower	Upper	
Age group								
5–9 years	105	29	13	53	1.40	1.01	1.93	0.042
10–14 years	233	35	19	55	1.80	1.05	3.08	0.034
15–21 years	60	23	10	45	1.00			
Material of floor at home								
sand	261	40	23	60	3.10	1.48	6.49	0.003
smeared mud	100	31	16	52	2.05	1.12	3.74	0.020
stone/cement	37	18	6	43	1.00			
Source of water at home								
other	5	56	31	78	6.03	3.32	10.95	<.0001
community tap/ well	333	20	11	34	1.18	0.53	2.64	0.680
tap on compound	60	17	6	42	1.00			
Number of times feed washed								
no answer	33	7	1	44	0.20	0.03	1.44	0.110
less than daily	11	62	45	76	4.19	1.87	9.38	<.0001
once a day	72	35	22	50	1.37	0.82	2.28	0.234
twice a day	282	28	16	44	1.00			
Chicken at home								
present	379	19	9	36	0.34	0.20	0.58	<.0001
absent	19	41	19	67	1.00			

*out of all tungiasis cases interviewed

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kilometres apart [17]. The disease burden was highly aggregated even within an individual school, with more than half of the cases having only a few embedded sand fleas but a minority being severely affected. The overall prevalence of 48% of all screened school-aged children was twice as high as the prevalence in the simultaneously implemented household study [11], reflecting the high proportion of the most affected age group in the school-based study. As has been shown before in Brazil [17], Uganda [18], Nigeria [19], and Kenya [20, 21], school-aged

Table 7. Population Attributable Fractions. (OR: Odds Ratio, AR: Attributable Risk, PAF: Population Attributable Fraction).

Factor	Any Infection				Heavy Infection			
	OR	AR	% exposed among cases	PAF (%)	OR	AR	% exposed among cases	PAF (%)
Classroom floor of sand	2.99	0.67	21.5	14.3				
Home floor of sand	1.88	0.47	65.6	30.7	3.1	0.68	80.3	54.4
Home floor smeared mud					2.05	0.51	16.9	8.7
Never using soap for washing feet	6.3	0.84	6.1	5.1				
Only using soap for washing sometimes	1.6	0.38	57.2	21.5				
other water source					6.03	0.83	4.2	3.5
wash less than daily					4.19	0.76	5.6	4.3
Do not own a chicken					5.19	0.81	9.9	8.0

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children below the age of 15 years were the most affected by tungiasis and boys were twice as likely as girls to have the disease.

The risk factor interviews as well as the follow up examinations after the long school holidays suggest strongly that the highest risk of disease is associated with the socio-economic circumstances of the individual student at home. Whilst an unsealed, natural sand or soil floor of a classroom came out as an independent risk factor in the analysis it is important to note that such classroom floors were only present in two schools where the majority of pupils came from homes that had unsealed floors. The calculation of the PAF indicates that mild to moderate tungiasis could be reduced by a third, and severe tungiasis by over a half, if homes (sleeping places of children) had sealed floors, whilst approximately a seventh of the cases could be prevented by sealing classroom floors in schools. The presence of unsealed floors at home, has been previously indicated as an important risk factor for the disease [13, 21, 22], and can only be a consequence of the biology of the sand flea, with egg, larval and pupal (off-host stages) development taking approximately three weeks and requiring shaded, dry, loose soil or sand [4, 5]. Such unsealed floors provide a constant supply of the sand fleas searching for hosts as soon as they emerge as adults. This finding also corroborates the assumption that in settings where the prevalence of tungiasis is stable the whole year round, the transmission mainly takes place inside the house, particularly in the room where children sleep [1].

Neither the condition of the school uniform, nor wearing shoes potentially protecting against host-seeking sand fleas [23] was independently associated with tungiasis, however, the combination of a torn uniform and the absence of shoes can be considered an indicator of the poverty level or care given to the child at home. Complex interactions between risk factors suggest underlying behavioural differences in the care given by parents and guardians and/or hygiene behaviour expressed in boys and girls. Boys with torn uniforms were four times more likely to be affected by the disease than girls wearing uniforms in equally poor condition.

Whilst the frequency of washing was not associated with tungiasis, the availability of piped or well water within the homestead and the use of soap when washing was strongly associated with reduced risk. Both factors might be linked to the socio-economic status of the family to afford piped water and soap, but also to behavioural characteristics of the care givers and children, as already noted in the household study [18].

The higher risk of infection and severe disease observed for boys between the ages of 10 and 14 years may be a reflection of their hygiene practices, being less likely to wash daily, particularly with soap than girls in the same age group. Whilst such a sex-specific association was not detected in the analysis in the current study, previous studies using interviews and observation in other countries have found boys to have poorer skin hygiene than girls [24]. A recent study examining the relationship between socioeconomic status and WASH practices in India also highlighted the fact that over 80% of mothers did use soap to wash themselves but only 20% used soap to wash their children [25].

The data from before and after school holidays, whilst a small dataset, highlighted a number of findings that are significant and warrant replication in future. Not only did the overall prevalence of tungiasis increase after the holiday, there was also a significant increase in the number of manipulated lesions. These are the sores and cicatrices that remain after an embedded sand flea has been purposively extracted with a sharp instrument and are a clear indication that the person recently had a viable embedded sand flea. The likely explanation is that the children have acquired more sand fleas whilst spending more time at home during the holiday, but they or a caregiver have extracted them. There was a significant interaction between the number of manipulated lesions and girls, again suggesting differential hygiene and caring behaviours. Teasing apart these complex linkages of economic status and behavioural traits will be important in future studies and might indicate school-aged boys to be an important target for prevention programs.

Surveys in other countries have identified tungiasis as a zoonosis with the involvement of dogs [13] and pigs [26, 27] in disease transmission. Pigs are not frequently kept in communities in coastal Kenya (only four students in the survey reported owning pigs), whilst goats and dogs were relatively common with 75% and 30% of students reporting household ownership, respectively. However, neither the previously published household study [11] nor the here presented school survey identified the possession of any animal species to be a risk factor. Whether this is an indication that transmission in these coastal communities is purely intradomiciliary and does not involve an animal reservoir needs further investigation by examining livestock and companion animals for tungiasis. The current school survey did identify the absence of chickens in a household as a risk factor for severe disease, which may simply be another reflection of extreme poverty as a risk factor, which needs to be studied however more systematically.

The fact that the same household risk factors were identified in this study by asking the children about their homes, as in the corresponding household study where adults were interviewed, and observations made, suggests that school-based surveys are a reasonable alternative to the more expensive and time-consuming household surveys and can be used for nationwide evaluation of tungiasis prevalence. Modelling based on past household surveys with full age profiles will enable extrapolation to the whole population. School-based surveys have the advantage of a high concentration of at-risk subjects to survey during day time when there is good light for examinations. To be able to examine all house occupants for tungiasis a team must visit during evening hours and at weekends, and still many family members may be absent. Houses may be far apart, and therefore surveying costly to achieve suitable sample sizes.

Targeting school-aged children in school for diagnosis and treatment of tungiasis, using recently evaluated safe and effective treatment options, namely dimeticone or neem oil [2, 28, 29], might be the most cost-effective way to reduce the disease burden given that the affected resource-poor communities do not have access to optimal medical care and limited ability to pay for expensive medications. However, the treatment must be provided every time a new infection in a child is detected by the teachers to prevent the life cycle being introduced into classrooms with a cracked or natural sand/mud floor, and to break the cycle at home. The disadvantage of conducting surveys and treatment programs only in schools means the most severely affected children who cannot walk to attend school, the elderly and disabled, who also tend to have severe infections, will be missed.

This factor was a possible limitation of the study, possibly causing bias in the study findings. However, the study included a similar proportion of severe cases to that seen in the household survey (11% and 15% respectively), so any effect on outcomes is likely to be minimal. The higher proportion of severe cases in the household survey was more likely to be due to the inclusion of the elderly who tend to have more severe infections [11].

Another limitation of the study was the low number of schools with non-cemented floors that were able to be included in the study, and that the one school that was entirely dirt floors, was the only private school, with the majorty of children in the lower age groups. However, any potential confounding was adjusted for in the statistical modeling.

Observations from our study suggest that up to 70% of tungiasis cases may be prevented through simple prevention methods, namely washing feet at least once a day with soap and installing hard floors in homes and schools. Hence, foot washing needs to be incorporated into hygiene and sanitation education campaigns of the current global efforts to achieve Sustainable Development Goal 6; "by 2030, achieve access to adequate and equitable sanitation and hygiene for all". Tungiasis has been implicated to impact children's learning capacity [9], consequently, there is a clear role and need for schools (head teachers and class teachers), public health officials, community health workers and NGOs to educate in and enforce good hygiene practices, particularly the use of soap for daily washing of feet. Furthermore, acknowledging that sealed classroom floors can contribute to tungiasis reduction, governments and education officials need to make the cementing of all classroom floors a priority, along with adequate water supplies and provision of soap for washing.

The installation of hardened floors in family homes is not as simple as it sounds, and requires research and potentially government investment. Those resource-poor, marginalized families affected by tungiasis cannot, under most circumstances, afford the cost of a cement floor, which in Kenya costs a minimum of $200 for a typical rural house of 6 x 4 m. In discussions with community members, it was highlighted that in the past communities used traditional methods for hardening floors such as regular smearing with a mix of soil and cow dung and termite mound soil, but these methods have ceased, and floors are no longer hardened (Elson, personal communication). Clearly there is a need for research into understanding why house floors are not hardened with the simple, cheap methods currently available, as well as developing alternative, locally available and affordable floor technologies that the most resource-poor families can install themselves.

Supporting information

S1 Annex. Information leaflet and consent form.
(DOCX)

S2 Annex. STROBE checklist.
(DOCX)

S3 Annex. Database-tungiasis examination and classroom characteristics.
(XLSX)

S4 Annex. Database-tungiasis before-after school holiday in KS1.
(XLSX)

S5 Annex. Database- tungiasis risk factor interviews.
(XLSX)

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Writing – original draft: Lynne Elson, Susanne Wiese, Ulrike Fillinger.

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Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

<u>Komplette Publikationsliste</u>

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1) Wiese S, Elson L, Feldmeier H. Tungiasis-related life quality impairment in children living in rural Kenya. PloS Neglected Tropical Diseases. 2018;12(1):e0005939.
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3) Elson L, Wiese S, Feldmeier H, Fillinger U. Prevalence, intensity and risk factors of tungiasis in Kilifi County, Kenya: II. Results from a school-based observational study. PLoS Neglected Tropical Diseases. 2019;13(5):e0007326. doi: 10.1371/journal.pntd.0007326.
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