SEX-RELATED MORTALITY AFTER BURNS: A SCOPING REVIEW IN THE SADC-REGION

LA MORTALITÉ LIÉE AU SEXE APRÈS UNE BRÛLURE : UNE REVUE DE CADRAGE DANS LA RÉGION DE LA SADC

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SUMMARY. Findings on mortality by sex after burns in low- and middle-income countries (LMICs) are contradictory and, where differences have been described, the reasons are often based on speculation and not on the analysis of factors that could have affected the outcome, such as patient or injury characteristics or provided care. Since the paucity of studies on burns from single LMICs is notorious, merging data from neighboring countries with similar socio-economic backgrounds might provide a larger dataset, contributing to identifying recurrent causes. This scoping review aimed therefore to analyze differences in mortality after burns between the sexes, as well as to identify aspects that could explain possible differences, in countries belonging to the South African Development Community (SADC) region. Studies in English published between 2010 and 2020 were identified according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines by searching PubMed and/or Medline, Clinical Trials and Cochrane Library, and using the screening tool "Covidence". The 13 included studies could not consistently show association between sex and mortality after burns, but contradictory findings. In the case of differences in outcome between the sexes, explanations were mainly based on speculation (e.g., hormonal differences, self-harm intention), while rarely burn specific factors were reported and included in the analysis of the mortality risk. This study indicates the need for prospective burn specific data collection in LMICs that would contribute to identifying factors associated with death.

Keywords: burns mortality, sex-related difference, SADC region, review

RÉSUMÉ. *Les résultats concernant la mortalité par sexe après brûlures dans les pays en développement (PED) sont contradictoires et, en cas de différence, les raisons sont souvent spéculatives et non basées sur l'analyse de facteurs qui auraient pu affecter le résultat, tels que les caractéristiques du patient ou de la brûlure ou les soins fournis. Étant donné la rareté des études sur les brûlures dans les PED, la fusion des données de pays voisins ayant un contexte socio-économique similaire pourrait fournir une base de données plus large contribuant à l'identification des causes récurrentes. Cette revue de cadrage visait donc à analyser les différences de mortalité après brûlures entre les sexes, ainsi qu'à identifier les aspects qui pourraient expliquer d'éventuelles différences, dans les pays appartenant à la région de la Communauté de développement de l'Afrique australe (SADC). Les études en anglais publiées entre 2010 et 2020 ont été identifiées selon les Preferred Reporting Items for Systematic Reviews and Meta-Analysis en effectuant des recherches dans PubMed et/ou Medline, Clinical Trials et Cochrane Library, et en utilisant l'outil de sélection "Covidence". Les 13 études incluses n'ont pas pu montrer de manière cohérente l'association entre le sexe et la mortalité après brûlures, mais des résultats contradictoires. Dans le cas des différences de résultats entre les sexes, les explications étaient principalement spéculatives (par exemple, différences hormonales, intention d'automutilation), tandis que les facteurs spécifiques aux brûlures étaient rarement rapportés et inclus dans l'analyse du risque de mortalité. Cette étude indique la nécessité d'une collecte prospective de données spécifiques aux brûlures dans les PED qui contribuerait à identifier les facteurs associés à la mortalité.*

Mots-clés: *mortalité par brûlure, différence liée au sexe, région SADC, revue*

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Introduction

Overall, less women die from trauma than men, and hormonal difference has been indicated as one of the main reasons.[1-5] In burn injuries, instead, the World Health Organization (WHO)[6] reported that "females have slightly higher rates of death from burns compared to males", suggesting differences in behavior pattern and risk exposure between the sexes as the causes of this divergence, but at the same time highlighting the paucity of studies on the topic. It is undeniable that socioeconomic factors have an impact on burn incidence, severity and mortality,[7,8] and in fact, most deaths by burns occur in low- and middle-income countries (LMICs).[6,9] However, since the extent of literature output on burns in LMICs is limited,[10,11] whether or not there are differences in outcome between the sexes is still understudied. Merging data from neighbouring countries with similar socio-economic settings and comparing findings can contribute to filling knowledge gaps in a specific region.

The Southern African Development Community (SADC) is an "inter-governmental organization that promotes sustainable and equitable economic growth and socio-economic development" among its member states. The SADC Vision aims to improve the quality of life of the people living in the region, rationalizing and merging resources.[12] The SADC consists of sixteen Sub-Saharan countries with relatively similar socio-economic context, including disparities in health care accessibility.[13] Identification of differences among member states is a necessary step in the harmonization process advocated by the SADC Vision.

The aim of this scoping review was therefore to study possible divergences between the sexes in mortality after burns and their causes in the SADC region between 2010 and 2020.

Materials and methods

Search strategy

Studies reporting in-hospital mortality after burns by sex in country members of the Southern African Development Community (SADC) were identified by searching PubMed and/or Medline, Clinical Trials and Cochrane Library, using the keywords listed in *Appendix 1*. The search strategies were designed and executed by all authors. Inclusion criteria were articles in English available in full text, conducted in SADC-countries between 2010 and 2020 that included synonyms and keywords for the following search concepts: burns, scalds, thermal injury, sex, female, male, women, men, boys, girls, mortality, death. SADC countries were defined by the PubMed Mesh-term "Southern African Development Community" and included: Angola, Botswana, Comoros, Democratic Republic of Congo, Eswatini, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, United Republic of Tanzania, Zambia, Zimbabwe. Exclusion criteria were opinion and editorial pieces, case reports, systematic/scoping reviews, consensus guidelines and papers with the wrong setting (not SADC countries), and studies that did not report in-hospital mortality by sex among burn patients.

Study selection

This scoping review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. After creating the project in Covidence, screening was done by two independent reviewers, who applied eligibility criteria to all titles and abstracts. In case of disagreement between the reviewers, a third reviewer solved the conflicts.

Data extraction and analysis

Data extraction from full text was performed. Outcome of interest was in-hospital mortality and extracted variables were grouped in four themes: **study characteristics** (including year of publication, country, objectives of the study, study type, study setting), **demographic characteristics** (number of patients by sex, age of patients, presence of co-morbidity, origin of patients, educational level), **burn characteristics** (cause of burn, mechanisms of burns, site of the burn injury, percentage of the total body surface area burned (TBSA%), location of the burn on the body, presence of full thickness burns, presence of inhalation injury), and **burn care** (use of traditional medicine, time to seeking care, length of stay (LOS), provision of surgery during the

admission, complications during admission). All data were analyzed with thematic analysis and descriptive statistics. A map of the SADC region within highlighted countries from which the studies were conducted was made.

Results

Study characteristics

The electronic research identified a total of 2017 papers. After exclusion of 236 duplicates, 1781 articles were screened at abstract level, and 75 of them were eligible for full text examination. Among the 75 studies, a further 62 were excluded because older than 10 years (n=21), the country was outside the SADC region (n=1), they did not look specifically at burns patients (n=2), in-hospital mortality was not reported (n=5) or not by sex (n=13), they did not report data relevant for the scope of this review (n=6) or investigated outcomes were outside this paper´s purpose (n=2), they were literature reviews (n=3), only an abstract was available (n=8) or they had wrong PDF (n=1). Finally, 13 articles were included for data extraction and analysis (*Fig. 1*)**.**

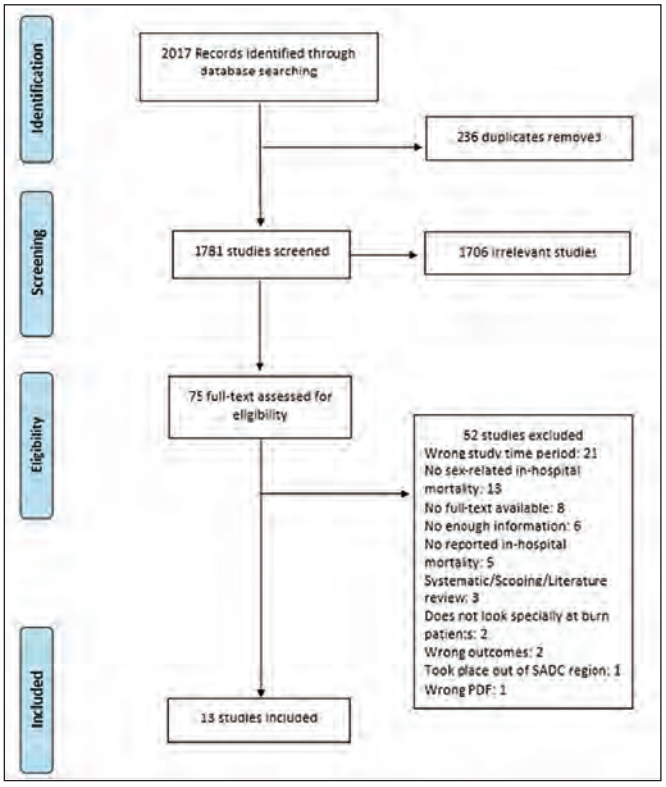

Fig. 1 - Prisma flow chart describing the selection process

All 13 papers came from three of the 16 SADC countries: Malawi (7 studies, 54%),[14-20] South Africa (5 studies, 38%),[21-25] and United Republic of Tanzania (one study)[26] (*Fig. 2*). All studies were retrospectively designed and were published between 2013 and 2020, with a maximum of 6 papers published in 2020 (46%). Three papers collected data from medical records,[21,22,25] nine from burn unit registries and databases,[14-20,24,26] and one from both medical records and burn unit database.[23] Only three studies were conducted at dedicated burn units,[21,23,24] while the rest analyzed data of patients with burns managed at general surgery services. The duration of the study period varied between 12 months and 112 months, with a median duration of 24 months (IQR: 15-48 months) (*Table I*).

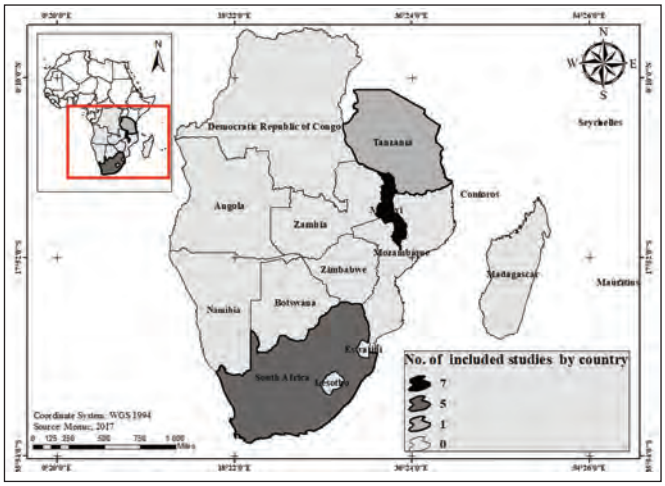

Fig. 2 - Map of SADC countries and studies involved in our scoping review (SM, 18/09/2021, Arcgis 10.7).

In-hospital mortality

Overall, in-hospital mortality of patients with burns admitted for care varied between 0.3% and 21%, with a median in-hospital death of 16% (IQR 7.1-17.8), but only seven studies described explicitly the rate of deaths between the sexes.[14,16-18,22,23,25] In five of them, most of the deaths were males (55% IQR: 48.75-59.2), while the contrary was found in two studies (45% IQR: 40.2-51.25).[17,25] The statistic difference in mortality by sex was calculated in 7 studies: four of them could not find a significant difference between the sexes,[16,19,20,26] two showed that females were more likely to die than males, while one study stated the con-

Table I - Summary of study characteristics of the 13 studies included in the review

	First author	Year of publication	Country	Study design	Health facility	Period of study	#tot patients	#female	(Mean or median) TBSA%	#Female deaths/#tot deaths	Length of stay median (in days):	Observation
1	Allorto	2020	South Africa	Retrospective register study	Pietermaritzburg Burn Service	March 2016 to February 2019	1484	671				Did not report sex-related in-hospital mortality.
2	Boissin	2019	Sweden South Africa	Retrospective investigation	The adult burns centre at Tygerberg Hospital in Cape Town	2015-2016	372 patients included in mortality analyses = 269	122			20	Mortality was significantly associated with being female (3.77)
3	Boschini	2014	Malawi	Retrospective (of prospectively collected burn data registry)	Kamuzu Central Hospital (KCH)	July 2011 to December 2012	435	205	Mean (in percentage) Overall (19 ± 17.8)	No seizure group (36/181:17%) - Seizure group (2/19:11%)	(23 ± 33.8)	
4	Brink	2018	South Africa	Retrospective observational review	Red Cross War Memorial Children's Hospital	January 2013 to December 2016	548	234		0/2	1-1.6	
5	chelidze	2016	Tanzania	Retrospective study	Sekou Touré Regional Referral Hospital (STRRH)	March 2013 to June 2014	211	85	8.0% (5.0–13.4)	Not reported	8.5 (4–14)	
6	Christofides	2020	South Africa	Observational retrospective study	Chris Hani Baragwanath Academic Hospital (CHBAH) Adult Burns Unit (ABU)	January 2005 to the end of December 2015	2055	687	15%	192/433	Not reported	
7	Gallaher	2020	Malawi	Retrospective analysis of prospectively collected data	Kamuzu Central Hospital (KCH)	May 2011 to July 2019	1689	704	Mean (in %): (16.4 ± 12.5%)		20.3 ± 25.3	Did not report sex-related in-hospital mortality. No statistical difference in mortality males vs females
8	Grudziak	2017	Malawi	Retrospective	Kamuzu Central Hospital (KCH)	July 2011-May 2016	1353	603	15 (8.5, 24)	Not reported	13 (7, 31)	
9	Grudziak	2017	Malawi	Retrospective review	Kamuzu Central Hospital (KCH)	July 2011-May 2016	823	383	15% (9, 23)	41/135	11 (7, 24)	
10	Purcell	2020	United States Malawi	Retrospective analysis	Kamuzu Central Hospital (KCH)	May 2011 to August 2019	1768	783	14 (8 - 21)	Not reported	12 (6 - 25)	
11	Purcell	2020	Malawi	Retrospective	Kamuzu Central Hospital (KCH)	May 2011-December 2019	1904	839	9.74 (0.5 – 100)	153/309	11 (6-24)	
12	Smith	2016	South Africa	Retrospective study	Edendale Hospital	July 2013 to June 2015	748	328	9.74 (0.5 – 100)	32/53	Not reported	
13	Tyson	2013	Malawi	Retrospective analysis	Kamuzu Central Hospital (KCH)	Between June 2011 and December 2012	454	208	18.5% (± 17.4)	16%	Not reported	

trary.[21,23,24] Reasons for this discrepancy were not explained by data, but authors speculated about the role of hormonal differences, about self-harm intention, which is associated with poorer prognosis and is most frequent in women, and about health care organization´s intrinsic factors that imply that women are treated and discharged differently compared to men (*Table II*).

After adjustment for other factors, in-hospital mortality was independently associated with female sex in two studies (OR: 3.30,[24] and OR 3.79[21]), and with male sex in one (OR: 0.46).[23]

Table II - Characteristics of patients, by sex

Characteristics	Female	Male	References
In-hospital deaths, %	55% IQR: 48.75-59.2 5	45% IQR: 40.2-51.25	(14,16-18,22,23,25)
Age, years	-	34 (IQR: 25-43)	(21)
TBSA%	15.0% (IQR: 8.0-23.0)	13.0% (IQR: 8.0-20.0)	(16)
Patients who received surgery, %	87% and 55.5%	13% and 44.5%	(22,24)
Length of stay, days	10 (IQR: 6-21)	12 (IQR: 6-27)	(16)

Data are number (%), mean (SD) or median (IQR)

Other factors investigated to understand their effect on mortality were TBSA%, age, burn mechanism, time to reach hospital, presence of inhalation injury, and the fact of being referred or not.[15,16,21,23,25,26] Among these factors, those associated with mortality were burns of large size, presence of inhalation injuries, accidental injuries, flame burns or scalds, patients admitted directly for acute burn care without being remitted from other facilities, and conservative treatment without surgery.[23,26] However, these factors were not adjusted for the sex of the patients. One study showed that admission after 24 hours was not associated with lethal outcome.[21]

Demographic characteristics

A total of 13,860 patients with burns were described in the 13 studies, and 8001 of them were males (58%), with a sex-ratio M/F of 1.36. In three studies, most patients were adults,[21,23,25] whereas in ten they were younger than 15 years of age.[14,16-21] Six studies focused exclusively on paediatric burns.[15,16,19,20,22,26]

No study reported the educational level of the patients, whereas their origin was stated by one study conducted at the burn unit of the Tygerberg Hospital in Cape Town (South Africa), which highlighted the predominance of urban patients (79%) among those admitted.[21] Seven studies discussed the presence of pre-existing medical conditions,[14,15,17,21,22,24] with seizure being the most frequently reported,[14,15,17,18,21,24] followed by malnutrition[15,17] and presence of HIV and tuberculosis.[22]

Burns characteristics

Mechanisms behind burns were reported by three studies, with accidental injuries being the most frequent, followed by assault and self-harm,[23,24,26] and according to two studies, more than 90% of injuries occurred at home.[22,26] The major causes of burns were scalds, followed by flame, electrical, chemical and contact burns.[14-20,22,26]

TBSA% was reported by almost all papers (n=12). In seven of them, it was not normally distributed, and median TBSA% varied from 8 (IQR: 5-13) to 15.4% (IQR: 8.5-24), with an overall median of 14% (IQR: 14-15), whereas in the four with normal distributed TBSA%, the mean varied from 9.7 to 19%, with an overall mean of 15.9% (SD 4.2). In one paper, women had higher median TBSA% than men (15.0% [IQR: 8.0-23.0] vs. 13.0% [IQR: 8.0-20.0]), but they did not show any statistical difference in terms of mortality.[16]

Three papers reported presence of full thickness burns in 34%, 41% and 46% of the patients, respectively.[21,24,25] Only one study described location of injuries on the body, with head and neck being the most frequently affected, followed by trunk and upper limbs.[21] Presence of inhalation injury was reported in four studies and it varied from 1.1% to 45.8% of patients.[21,22,24,25]

Burn care

Six papers highlighted that traditional medicine was used before reaching care at the hospital by a mean of 13% of patients (SD-3.125)[15,16,18-20] The time to seeking care at health care facilities was stated in nine studies: five showed that most patients were admitted to the hospital within the first 24 hours from injury,[14,17,20,21,26] whereas four reported that the majority were admitted more than 24 hours after injury.[16,17,19,24] Surgery was provided to a fifth of the burns (median provision of surgery

= 20.8% [IQR: [19-33.12]), as reported by eight papers.[14-17,19,22,24] Only one paper described the occurrence of in-hospital complications, such as sepsis, respiratory infections and skin graft failure.[22]

Among the 9 studies that reported the overall length of stay (LOS), one showed a normally distributed LOS (23 days [SD 33.8]),[19] one a mean of 1 to 1.6 days of hospitalization per each TBSA%,[22] and in the 7 studies in which LOS was not normally distributed, median LOS varied between 8.5 (IQR:4-14) and 20.3 days, with an overall median LOS of 12.5 days (IQR 11-20).[15-18,20,21,24,26]

Discussion

The impact of sex on mortality after burns in LMICs is still understudied. Previous international publications highlighting sex-related disparity in mortality have tried to explain it based on race, age, location of burns, presence of inhalation injury, TBSA%, proportion of self-intended injury, presence of comorbidities or differences in provided care,[27-34] but in some of them, sex was independently associated with death.[27,28,30,35] However, reasons for discrepancies, in the case there is a discrepancy, have not been systematically investigated and several hypotheses have been raised. With this scoping review, we identified 13 studies published in the last decade by countries listed in the Southern African Development Community (SADC), which reported mortality by sex,[14,15,24-26,16-23] and seven of them compared the difference between male and female.[16,19-21,23,24,26] Three have found female sex to be a factor independently associated with worse outcome,[21,23,24] whereas four studies did not find any sex-related difference in mortality after burns,[16,19,20,26] confirming what has been shown by the large body of literature.[11,36-40]

Among the studies included in this review, three speculated that females were more vulnerable after burn injury than men due to hormonal differences,[16,21,23] as assumed previously by other authors.[1,4,41,42] In animal models, authors reported immunosuppression post burn injury, proportional to the level of oestrogen, resulting in higher mortality in females compared to males.[41-44] In fact, the lack of sex-related difference in mortality among children and the elderly supports this hypothesis, since the low level of oestrogen in both pre-pubertal girls and post-menopausal women might suppress its effect on risk to die by burns.[27-29,37,39,45] Furthermore, previous publications have shown higher mortality after burns in adult women, between 20 to 69 years of age, an age range in which oestrogen level is still high.[27,28,39] Other authors ascribed discrepancies in mortality to metabolic differences,[16] such as lower hypermetabolism and catabolism after burn injuries in women, as compared to men.[39]

One of the included studies suggested that sex-related differences in treatment and discharge after burn injury may explain the difference in outcome,[21] as previously indicated by other authors.[35,46,47] However, this aspect has rarely been considered in patients with burn,[40] and no study in our review has analysed it in detail. Management of burns is not sex-specific, which is reflected by lack of sex-adjusted medical intervention in burn care such as rehydration formulas, excision, or skin grafting techniques that are not adapted to the sex of the patients.[48-50] Moreover, no disparities in mortality have been shown when the medical interventions were provided equally between the sexes in a high resource setting.[40]

One included study linked sex differences in mortality to a high proportion of self-harm burn injuries among women.[23] This was also suggested earlier by other authors.[51,52] However, this has been identified as a non-neglectable confounder, as after adjustment by logistic regression, intentionality of injury no longer appears to be a factor independently associated with death.[28,29]

Seven of the included studies adjusted the role of sex on outcome for other variables, such as age, burn location, TBSA%, presence of full thickness burn, presence of inhalation injury and burn mechanism,[16,19-21,23,24,26] while four used Pearson's or Fisher's exact tests, not finding any association between sex and death.[14,15,17,18] One paper focused on applicability of mortality prediction models in the South African population and did not analyze relation between sex and mortality,[25] whereas another was just descriptive.[22]

Finally, although some studies included in this review indicated sex-related differences in deaths by burns,[21,23,24] explanations of these findings were not evidence-based, but speculatory. A probable reason for this is the paucity in LMICs of systematic data collection in a dedicated burn registry, which is necessary to analyse the impact of injury- and patient-related factors on outcomes.[10,53]

Limitations

This study is not without limitations. Our review identified papers from only three of the 16 SADC countries, which limited the generalizability of our findings. A possible explanation is that we limited our search to publications in English, which might potentially exclude studies from non-English speaking countries. In fact, five SADC-countries have French as their official language and two Portuguese. None of the included papers came from these five states.

Another hypothesis could be that a country's income impacts their research output, with wealthy countries being more productive than poorer, as suggested previously.[10] Nevertheless, our review did not confirm this hypothesis. In fact, Malawi, which has one of the lowest gross domestic products (GDP) of the region, contributed the most with seven of the 13 included studies, followed by South Africa, which has the highest GDP with five studies, and Tanzania with one. Our study showed that systematic data collection more than a country´s GDP was the prerequisite necessary for conducting research, also in LMICs. In fact, all the seven studies from Malawi came from Kamuzu Central Hospital burn unit, a well-structured burn unit, which has collected data in a burn registry since 2011.

Another limitation is that many studies did not report and/or extensively analyse factors that could affect prognosis, such as inhalation injury (reported by four studies), presence of full thickness burns (reported by three studies), comorbidities (reported by seven studies), or origin of the patient (reported by one study). This may be attributable to the lack of methodical data collection, which makes it difficult to describe basic information.

Conclusion

Few publications investigated the role of sex on mortality after burns in the SADC-region, and the findings were controversial. Where a discrepancy was highlighted, explanations were predominantly based on speculation rather than data. Systematic data collection in a dedicated burn registry was associated with highest output, irrespective of the country's GDP. Implementation of prospective data collection on patient demographics, severity of injury and provided care would contribute to understanding possible discrepancies in outcome.

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Appendix 1

The search strategy in MEDLINE/PubMed

The following keywords were used: ("Burns"[Mesh] OR "burn*"[tiab] OR scald*[tiab] OR "thermal injur*"[tiab] OR "flame"[tiab] OR "electric*"[tiab] OR "chemical burn*"[tiab] OR "chemical injur*"[tiab] OR "acid burn*"[tiab] OR "acid inj*[tiab]) AND (death*[tiab] OR mortality[tiab]) AND ("SADC"[tiab] OR "Southern African development community"[tiab] OR "ANGOLA*"[tiab] OR "BOTSWANA*" [tiab] OR "COMOROS*" [tiab] OR "DEMOCRATIC REPUBLIC OF CONGO"[tiab] OR "CONGO*"[tiab] OR "ESWATINI*"[tiab] OR "LESOTHO*"[tiab] OR "MADAGASCAR*"[tiab] OR "MALAWI*"[tiab] OR "MAURITIUS"[tiab] OR "MOZAMBIQUE"[tiab] OR "NAMIBIA"[tiab] OR "SEYCHELLES"[tiab] OR "SOUTH AFRICA*"[tiab] OR "UNITED REPUBLIC OF TANZANIA"[tiab] OR "TANZANIA*"[tiab] OR "ZAMBIA*"[tiab] OR "ZIMBABWE*"[tiab]) AND ("gender"[tiab] OR "sex*"[tiab] OR "male"[tiab] OR "female"[tiab] OR "boy*"[tiab] OR "girl*"[tiab] OR "men"[tiab] OR "women"[tiab]) AND (2010[pdat] : 2020[pdat]).