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Review

The Race Against Time for the Enhancement of African National Strategic Plans in the Neuroblastoma Research Heterogeneity

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Abstract: The valuation of neuroblastoma research heterogeneity at African country level is unspecified. Therefore, the study assesses the heterogeneity of neuroblastoma research in 54 African countries and develops recommendations for national cancer-control plans. Metadata of peer-reviewed scientific publications allied to African neuroblastoma research were retrieved from the Web of Science™ Core Collection Database for bibliometric analysis. Comprehensive science mapping analysis and statistical analyses were performed with bibliometric online platform[2] and GraphPad Prism v. 10.2.3. This study revealed that African countries focused the neuroblastoma research publications mainly on the sustainable development goal of good health and well-being. The dominating research area in Africa is oncology followed by pharmacology. Only 26 of 54 African countries were accountable for total neuroblastoma research in Africa, with South Africa and Egypt contributing 61% of the whole continent's neuroblastoma research. Egypt, South Africa, Tunisia, Morocco, and Nigeria are the five most active African countries, and they are funded by different funding agencies internationally and domestically. The collected analysed data of this study draws special attention to heterogeneity and enduring upward correlating trajectory of Africa's neuroblastoma publication numbers, their citations, acquired funds, and countries' cooperation. Furthermore, this heterogeneity finding flags the necessity of developing a comprehensive strategic plan and implementation to cultivate neuroblastoma research as a fundamental part of each African country's national cancer control plans.

Keywords: cancer; neuroblastoma research; Africa; heterogeneity; bibliometric analysis

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1. Introduction

Neuroblastoma is a form of cancer that ascends from the embryonic sympathetic system [1]. It is primarily a paediatric cancer that is clinical, genetic, heterogeneous, and 50% of all patients can have metastases at the time of diagnosis [2–7]. Trustworthy paediatric cancer records are restricted, in size, to institutions in low- and middle-income countries [8]. This weakens the ideal analysis of data to reveal the real burden of neuroblastoma [9–11]. The neuroblastoma incidence was corrected by world-age standardized rates, where it was indicated that it ought to be 12% instead of less than 10% in Africa [11].

Nonetheless, in the previous decades, efforts of researchers in international and national collaborations steered amplified advances in our understanding of neuroblastoma [12,13]. Through the immense number, heterogeneity, and different quality of neuroblastoma allied publications, appraisal of the current state of research on this topic is essential for clinicians, researchers, strategic planners, and policymakers. Hence, we employed bibliometric analysis for extensive bibliographic metadata related to neuroblastoma research in Africa. Africa is a continent that is large, diverse, and it consists of 54 countries [14]. Out of the 54 countries, only 22 are presently ranked as low-income economies by the World Bank (2022–2023), indicating that they are the poorest countries (Table S1). Notwithstanding these developmental problems, populations throughout Africa are quickly ageing

and non-communicable diseases, particularly cancer, are nowadays becoming a foremost problem to economies and health systems [15,16]. Even the World Health Organization (WHO) has stated that a national cancer-control program ought to lessen cancer incidences and mortality rates, along with the advancement of the survival rates of cancer patients through the development of a national cancer-control that is systematic, impartial, and evidence based [17]. Relevant research context is crucial for directing more affordable, impartial, and improved results with the use of national cancer control plans through all the varied African national systems [18].

Thus far, policies on African cancer research have been undertaken through qualitative work around research barriers [19], descriptive, narrative lens directing to care [20], novel models for inclusive cancer care treatment [21,22], and weaknesses and strengths valuation of general types of cancer research at the country level [14,23]. However, the valuation of the comparative heterogeneity of specific types of cancer research namely, neuroblastoma research at the African country level is unspecified. Moreover, developing advanced policies for the enhancement of Africa's neuroblastoma research background is vital, then again it must be established on research data outputs which are mostly limited. This data must reveal the research heterogeneity situations for each of the 54 African countries. Thus, the aim is to assess the heterogeneity of the 54 African countries' neuroblastoma research and develop recommendations that may be adopted for each African country's national cancer-control plan. To convey to the reader, a literature review was included prior bibliometric analysis, for familiarity knowledge of the existing research in the field of neuroblastoma.

1.1. Historical Background

The paediatric cancer neuroblastoma was initially described by Dr. Rudolf Virchow in 1864, it was diagnosed as a glioma tumour in the abdominal cavity of a child [1,24]. German pathologist Felix Marchand originally identified the characteristics of tumours growing in the adrenal medulla, which is located above the kidneys, and the sympathetic nervous system in 1891 [24]. William Pepper first described stage (4S) neuroblastoma in 1901, stage 4S neuroblastoma spreads to the liver, skin, and bone marrow but not bone [24]. James Homer Wright was the first individual to name the tumour neurocytoma or neuroblastoma (Rothenberg et al. 2009) [25]. This name stemmed from his observations that roughly undifferentiated nerve cells, neurocytes, or neuroblasts were fundamental cells of the tumour [26]. He concluded that the ball-shaped neuroblasts called rosettes which surround fibrils that initiate in the adrenal medulla are similar, in morphology, to those that arise in the sympathetic nervous system, suggesting that neuroblastoma tumour originated from primitive cells [1,26]. From these findings, it has also been deduced that neuroblastoma is not a rare tumour, and it has been approximated that this specific tumour may contribute to an important group among gliomas, lymphomas, sarcomas, lymphosarcomas [1].

1.2. Epidemiology of Neuroblastoma

Neuroblastoma is one of the most common paediatric cancers which is usually diagnosed between infancy and 4 years of age and less than 5% of patients are above the age of 10 [27] Epidemiological measures show that between the years 1975 and 2017, the 5-year survival rate of patients with neuroblastoma increased from 86% to 91% for children under 1 year and for children aged between 1 and 14 years, the survival rate increased from 34% to 83% [28,29]. In high-income countries, neuroblastoma is the most common extracranial solid tumour that accounts for 6–9.7% of all cancers present in children at 15 years of age or younger [30–32]. In high-income countries found in Europe and North America the incidences of neuroblastoma were reported to be 10.5 and 11.6 cases per million, annually, in children below 15 years of age [33–36]. The estimated prevalence of Neuroblastoma in the world is 0.4 million. Approximately 650 children live with neuroblastoma in the United States of America every year [37]. The American SEER program has reported the incidence of malignancies in childhood between the years 2010 and 2015 for children in

the United States under the age of 15 was 16/100,000 [38,39]. In low- and middle-income countries that have a population-based registry, neuroblastoma is responsible for 1–3% of all paediatric cancers, however, its accurate incidence in Africa is not fully known [33]. Intraregional variations in incidence were observed in Argentina whereby a higher incidence was associated with high socioeconomic status areas [40]. Studies have shown that neuroblastoma accounts for approximately 8.6% of childhood cancers in the northwestern parts of Iran and 6.5% in the northeastern parts of Iran [41,42]. The neuroblastoma tumour has relatively low frequencies across all Asian countries [37,43,44]. Inconsistencies between the incidences of neuroblastoma in high, middle, and low-income countries may be due to late, suboptimal diagnosis and non-diagnosis, insufficient evaluation of pathology with immunohistochemistry, advanced imaging techniques, and unavailable resources in the infrastructure in low- and middle-income countries [30,33].

1.3. Classification of Neuroblastoma

Neuroblastoma patients may have different clinical, biological, and prognostic characteristics and one of the prognostic factors is the location of the primary tumour that may stem from the adrenal, abdominal/retroperitoneal, neck, thoracic, pelvic, or a different site [45]. Neuroblastoma tumours can metastasize from a primary location to one or more different sites in patients [46]. However, some cases of metastatic diseases can cause spontaneous differentiation or regression even amongst patients who do not receive any treatment [47].

Neuroblastoma tumours are staged as stage 1, 2A, 2B, 3, 4, and 4S using the International Neuroblastoma Staging System (INSS) and classification is based on multiple criteria such as the lymph node involvement, the degree of surgical excision of the primary tumour, dissemination to distant organs, the age of the infant, and the degree of bone marrow involvement [10]. A new classification system named the International Neuroblastoma Risk Group (INRG) was established for pre-treatment staging and risk assessment of neuroblastoma tumours through this system and the neuroblastoma tumours were classified as stages L1, L2, M, and MS [48]. These classifications were based on clinical criteria, and image-defined risk factors, Table 1 depicts the pre-treatment imaging which is classified based on the extent of the disease and image-defining risk factors INRG stage (L1, L2, M, and MS) [13,48,49]. The stage classified as MS encompasses patients with stage 3 primary tumours infiltrating the midline, and the MS group also comprises of children below the age of 18 months with limited dissemination. The 4S group, from the INSS is restricted to infants younger than 1 year of age [48,50].

Table 1. International neuroblastoma risk group (INRG) stages.

Stage	Description
L1	Localized tumour does not involve structures as defined by the list of image-defined risk factors and are confined to one body part.
L2	Loco-regional tumour with the presence of more image-defined risk factors.
M	Distant metastatic disease (except stage MS).
MS	Metastatic disease in children younger than 18 months with metastases confined to skin, liver, and/or bone marrow.

All data presented were adapted from references [12,48,49].

A more frequent occurrence in children below the age of 12 months with stage 1–3 and stage 4S neuroblastoma without myelocytomatosis-neuroblastoma (MYCN) amplification, is spontaneous regression [51,52]. However, data from a study displayed an infant with stage 4 neuroblastoma that showed spontaneous regression of the tumour at the metastatic site, this also encompasses meningeal metastasis after resection of the primary tumour [53]. The MYCN oncogene with extra copy alterations takes place when more than four copies are found in the tumour; this occurrence usually varies found between in 20–45% of neuroblastoma patients internationally [49,54]. Individuals that exhibit amplification in the MYCN oncogene are usually classified as high-risk, however, there is a rare exception

for patients with the L1 MYCN amplified disease that is resected and is stratified as non-high-risk, additionally, patients with the disease at 18 months or older are classified under high-risk neuroblastoma patients irrespective of the amplification of the MYCN oncogene [49,55]. Moreover, stage 3 and stage 4 patients with an MYCN amplified tumour exhibited the strongest association between time to first relapse (TTFR) and overall survival (OS) [2–7].

1.4. Potential Therapeutic Targets and Treatments

Numerous therapeutic targets have been identified due to a thorough understanding of molecular etiology, providing a variety of cutting-edge treatment options for high-risk neuroblastoma [56]. The transcriptomic and genomic profiles of neuroblastoma, currently, are guides for targeted therapy [56]. The molecular therapeutic targets anti-GD2 and ALK have been researched extensively internationally, however, many of neuroblastoma's molecular targets or pathways which include, p53/MDM2, GD2, MYCN, MIBG, PI3K/Akt/mTOR, BCL2, and RAS/MAPK signalling, have not been thoroughly researched as future prospects of therapeutic targets [56–69]. Preclinical and clinical trials are being conducted to discover and develop novel targeted medicines and combined therapies for the treatment of high-risk neuroblastoma. Currently, there are 148 completed neuroblastoma clinical studies listed on www.clinicaltrials.gov. Table 2 describes some investigational drugs in clinical trials and plant-based compounds for the treatment of neuroblastoma.

Table 2. Potential drugs in clinical trials and plant-derived bioactive compounds for the treatment of neuroblastoma.

Drugs in Clinical Trials (National Clinical Trial Number (NCT))			
Crizotinib [70]	DMFO (eflornithine) [71]	Sorafenib [72–74]	Vorinostat, 131I-metaiodobenzylguanidine (NCT02035137)
Lorlatinib (NCT03107988)	Ceritinib, ribociclib, trametinib (NCT02780128)	Prexasertib (NCT02808650)	Anti-GD2, GM-CSF, IL-2 [75]
Ceritinib (NCT01742286)	Trametinib, dabrafenib (NCT02124772)	Ribociclib (LEE001) (NCT01747876)	Dinutuximab, IL-2 [76]
Entrectinib (NCT02650401; NCT02097810)	Gefitinib [77–79]	Vorinostat [80]	Erlotinib [81]
Plant-based compounds-In Vitro Studies			
Flavonoids			
Genistein [82]	EGCG [21]	EGC [82]	Apigenin [82]
Apigenin [83]	DEDC [84]	Didymin [85]	Isoliquiritigenin [86]
Rutin [87]	Quercetin [88]	Butein [89]	Carnosic acid [90]
3,4-dihydroxybenzalacetone Caffeic acid phenethyl ester [91]	Genistein [82,92]	Isoliquiritigenin [93]	Luteolin [94]
Non-Flavonoid Polyphenols			
Curcumin [95]	Resveratrol [96]	Honokiol [97]	Prenyl hydroxy-coumarins [98]
Plant-based compounds-In vivo studies			
Flavonoids			
Didymin [85]	Apigenin [83]		
Non-Flavonoid Polyphenols			
Curcumin [99]	Resveratrol [100–102]		

2. Methods

2.1. Data Extraction

Peer-reviewed scientific publications metadata connected to African neuroblastoma research were extracted from the Web of Science™ Core Collection Database (Clarivate Analysis, Boston, MA, USA) on 16 July 2024. Only English-language literature was included and all authors searched, reviewed and checked the found literature. The search terms used were "neuroblastoma(s)" or "ganglioneuroma(s)" or "peripheral neuroblastic tumor(s)" or "ganglioneuroblastoma(s)". Publications issued from the year 2000 to 2024 were extracted using key metrics of publication number, citations, h-index, sustainable development, research area, and funds. Reviews, books, reprints, meeting abstracts, letters, proceeding papers, editorial material, early access, publication news, retracted data paper expression of concern publications, and biographical-items were excluded. Language restrictions were not obligatory. Moreover, in the context of this study, the excluded criteria comprised of publications wherein the majority of the authors or collaborators are non-African.

2.2. Data and Visualized Analysis

The UTF-8 format metadata were imported in "full record and cited reference" format into the bibliometric online analysis platform (http://bibliometric.com, accessed on 16 July 2024) for collaborative relationship analysis between countries/regions. Variables were expressed as sum and percentage. The citation average was expressed as mean ± SD. Their bibliographic data was downloaded and converted into an MS Excel spreadsheet for visualization analysis and statistical analysis. Statistical analyses were performed with GraphPad Prism v. 10.2.3 (GraphPad, La Jolla, CA, USA). The Pearson correlation coefficient (r) was used to test correlations between the number of research publications and awarded funds per African country. The closer the r was to +1 or −1, represented the higher the correlation between the two variables. A paired *t*-test was used and *p*-values of >0.05 were represented as statistically significant. R^2 or the coefficient of determination expresses how well the data fit the regression model.

3. Results

3.1. Overall African Countries' Publications, Citation Performance, and H-Index

The study incorporated a total overall 42,784 documents focusing on neuroblastoma research from 150 countries of the world, encompassing 29,880 original research articles, 2689 review articles published, and 54 book chapters. However, a total of 394 documents, including 335 original research articles, 58 review articles, and 1 book chapter were published in 28 African countries as depicted in Figure 1. The linear model displayed an increase in African research output between 2000 and 2023 (r^2 = 0.73). Year 2024 data was excluded from the linear model analysis because the data was extracted in July before the end of the year. In the early year 2000, the research output from Africa was less and commenced to increase after year 2011 and reached its highest peak in the year 2022 (*n* = 43; 11.67%) (Figure 2). The publication average of 15.38 ± 13.21 from the year 2000 to 2024.

In the viewpoint of citation performance from 2000 to July 2024, the total citation was 8482, and without self-citations the total was 8338 and the citation average was 21.53 ± 3.63. The citation of the published research outputs for the year 2024 (*n* = 674; 7.95%), was lesser compared to the period from 2000 to 2023. This was due to recently published outputs which were not cited considerably when data was extracted for this study. The highest citation reached its peak in the year 2022 (*n* = 1.295; 15.25%), and the number of multi-authored published research outputs increased significantly from the year of 2000 to 2023 (r^2 = 0.84). There was a correlation (r = 0.941; *p* = 2.398; r^2 = 0.089) between the published research outputs and the number of citations. Moreover, the overall h-index of Africa is 44 in the research field of neuroblastoma.

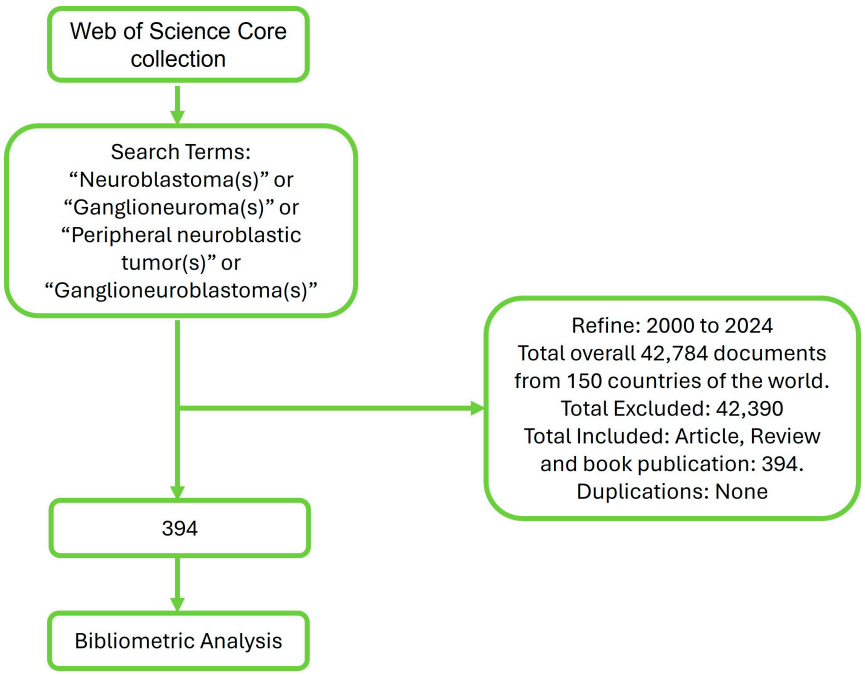


Figure 1. Diagram of Study Selection.

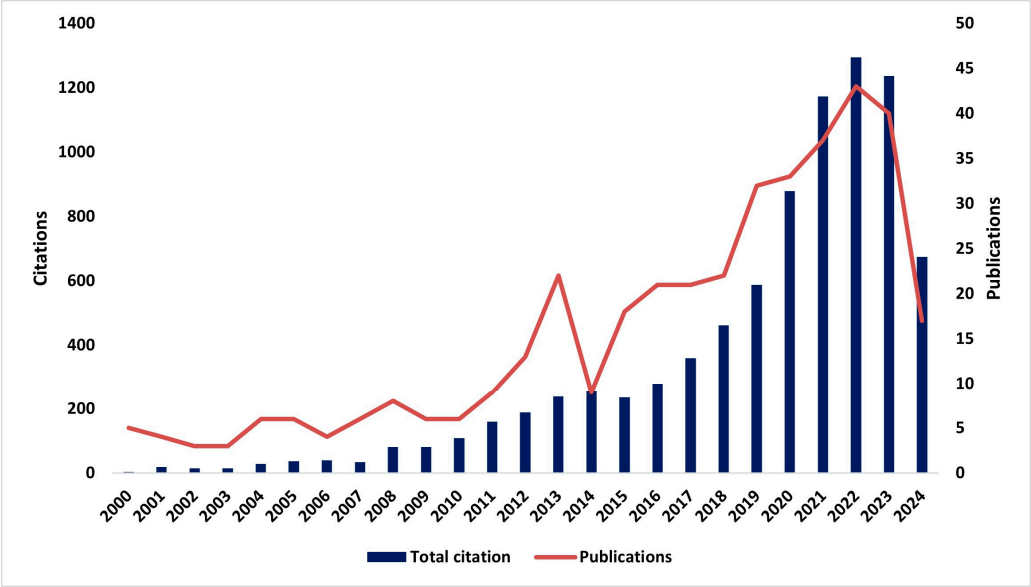
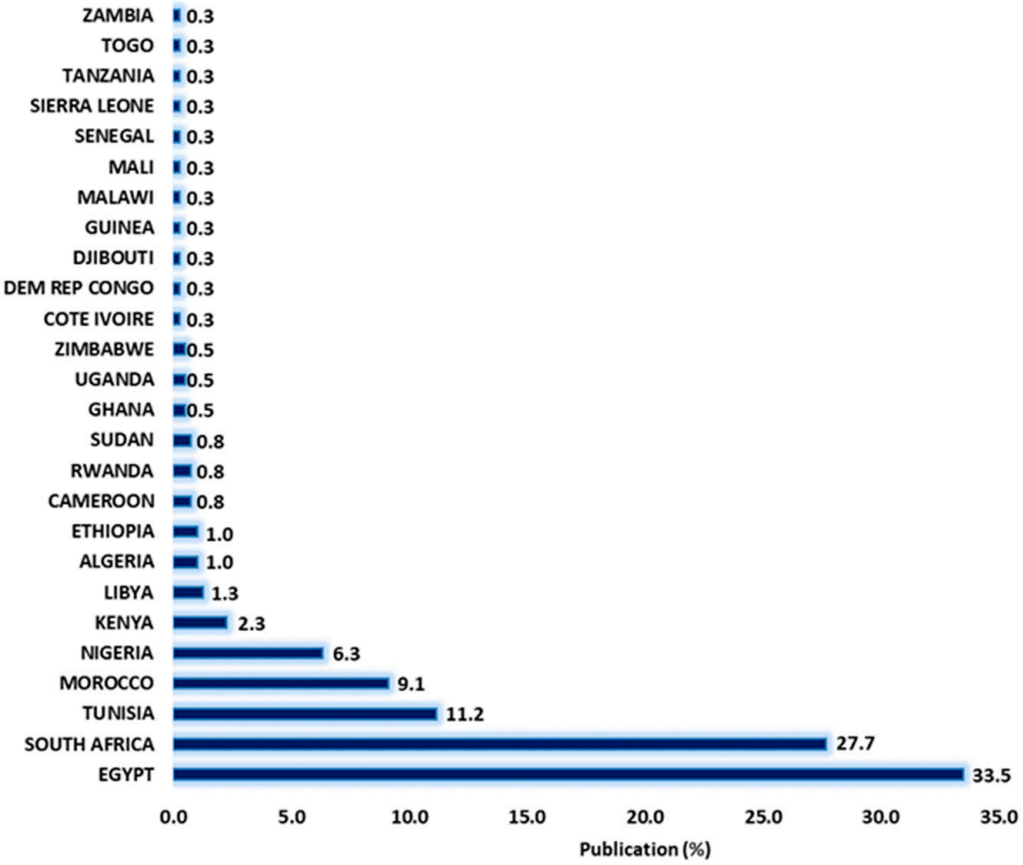


Figure 2. The overall annual research publication on neuroblastoma and citation performance of African countries from the year of 2000 to 2024.

3.2. African Countries' Research Activity and Sustainable Development

The top five African countries with high research activity are Egypt (n = 132; 33.5%), South Africa (n = 109; 27.66%), Tunisia (n = 44; 11.17%), Morocco (n = 35; 9.14%) and Nigeria (n = 25; 6.35%). Out of 54 countries, the exciting neuroblastoma research publications records for 25 African countries namely Egypt, South Africa, Tunisia, Morocco, Nigeria, Kenya, Libya, Algeria, Ethiopia, Cameroon, Rwanda, Sudan, Ghana, Uganda, Zimbabwe, Cote Ivoire, Djibouti, Guinea, Malawi, Mali, Senegal, Sierra Leone, Tanzania, Togo and Zambia (Figure 3a).



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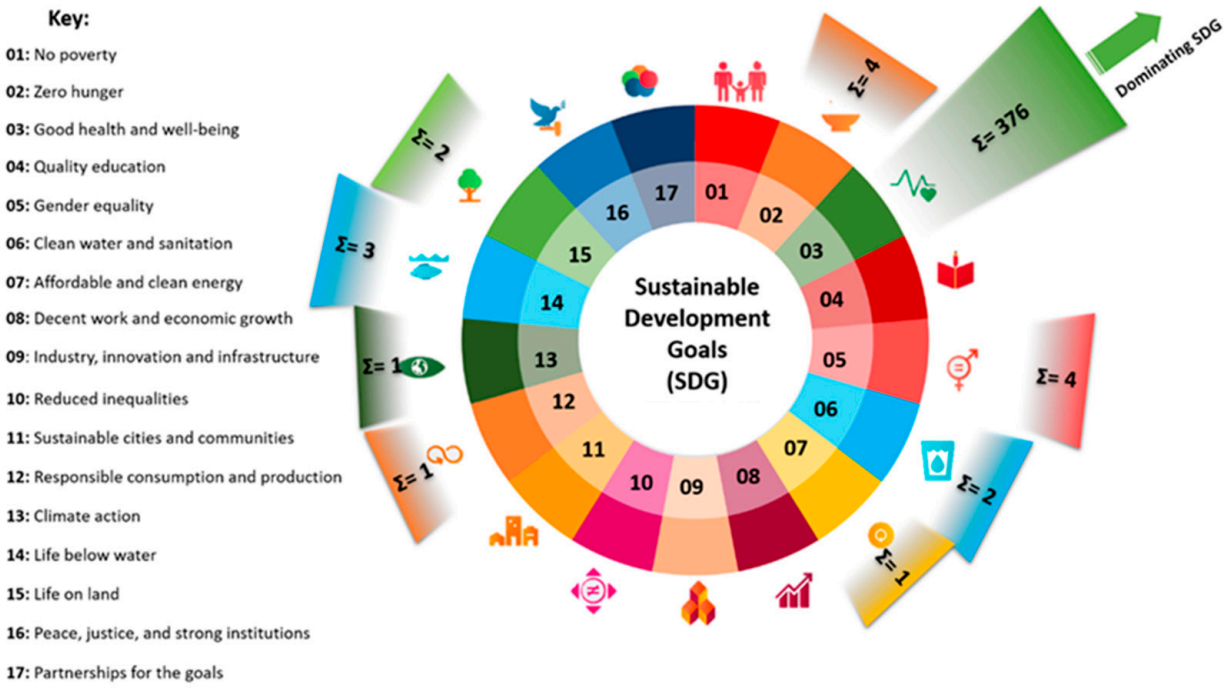


(**b**)

Figure 3. Publication performance of African countries in the neuroblastoma research field from the year of 2000 to 2024, presented as: (**a**) research activity; (**b**) sustainable development goals.

In terms of peace and prosperity for people and the planet, in this study, African countries focused the research publications mainly on the sustainable development goals of good health and well-being, zero hunger, partnerships for the goals, reduced inequalities, clean water and sanitation, and gender equality. These SDGs are, in one form or another, intertwined with the livelihood of neuroblastoma patients. Minimal progress and in some instances, there is complete stagnation in terms of research related to other sustainable development goals. This stagnation is attributed to the lack of paediatric oncology services in some African countires Figure 3b, displays the 17 SDGs that are currently present and there are more than six SDGs that correlate to neuroblastoma indirectly. Six SDGs are discussed and how they relate to neuroblastoma.

3.3. African Countries Dominate Research Areas and Funds

The overall dominating research area (RA) in Africa is oncology (n = 68, 11.26%), followed by pharmacology (n = 64, 10.75%), as depicted in Figure 4. Countries that publish research papers mostly in the research area of oncology are South Africa, Morocco, and Mali while Egypt, Algeria, Cameroon, and Togo follow closely. The published papers are mostly related to the pharmacology research area. In comparison to areas not directly related to neuroblastoma, research areas that are less predominant with 0.17% (n = 1) are crystallography, emergency medicine, gastroenterology, herpetology, microscopy, obstetrics-gynaecology, orthopaedics, polymer science, transplantation and allergy (Figures 4 and 5). This data outlines the funding ratio for neuroblastoma and other science disciplines. These disciplines may not be directly related to neuroblastoma, however, the disciplines may intertwine with neuroblastoma under the umbrella of drug discovery, improved diagnostic techniques or methodologies, regenerative medicine, the possible discovery of compounds in search of remedial treatments, effects of neuroblastoma on pregnant females and fetal developments, effects of neuroblastoma on bone development in children and many other criteria that fall under this umbrella. Possible collaborations between experts in these multiple disciplines on extremely intricate and challenging neuroblastoma cases may lead to potential solutions for adverse effects of neuroblastoma.

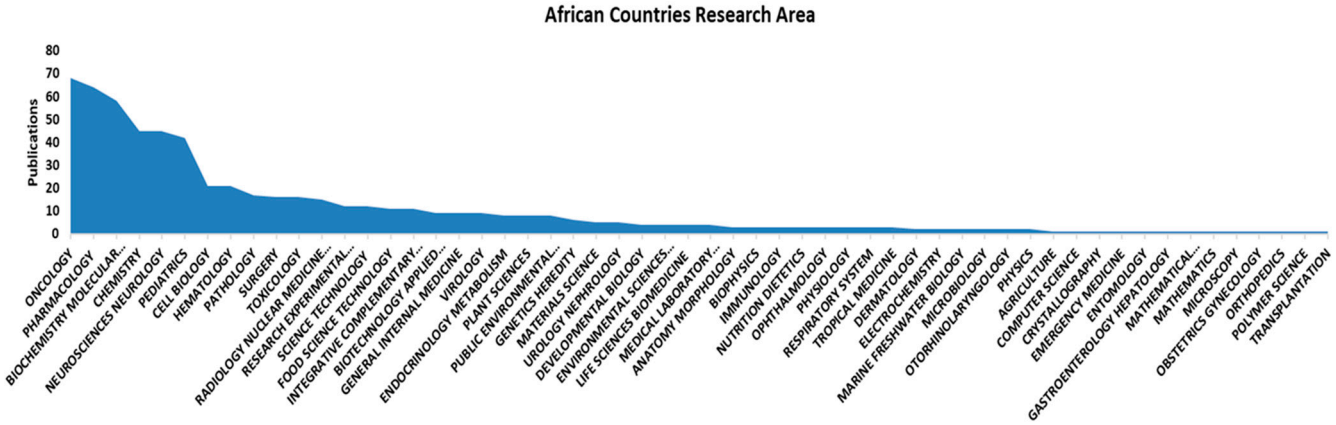


Figure 4. Overall performance of Africa's neuroblastoma research publications based on different research areas from the year of 2000 to 2024.

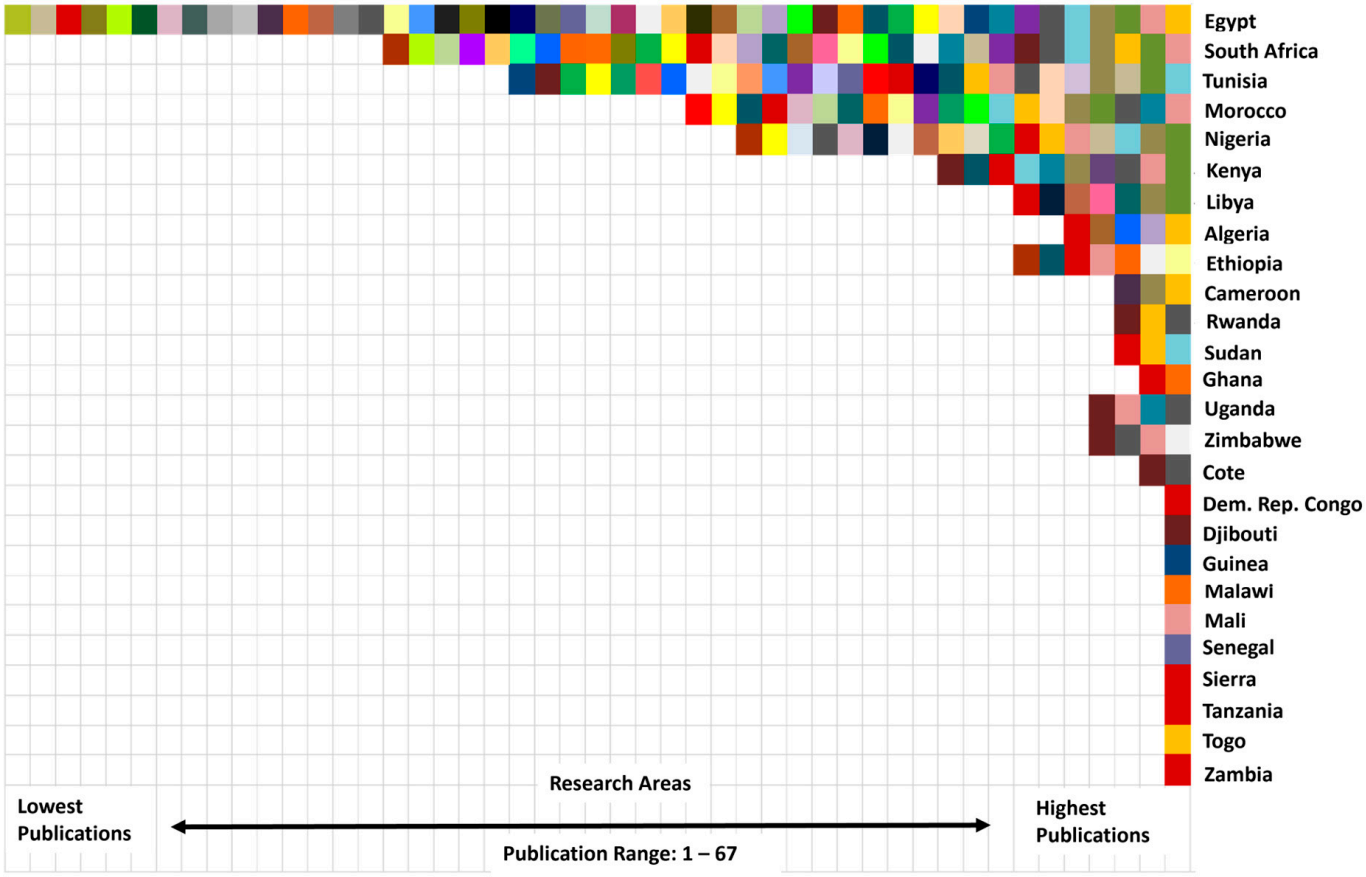


Figure 5. Dominant and less dominant research areas under the neuroblastoma research field in different African countries from the year 2000 to 2024.

Moreover, there is a large degree of inevitable involvement of Egypt (n = 47 RA), South Africa (n = 33 RA), Tunisia (n = 27 RA), Morocco (n = 21 RA), Nigeria (n = 18 RA), Kenya (n = 10 RA), Libya (n = 7 RA), Algeria (n = 5 RA, Ethiopia (n = 7 RA) in more/equal to five ($\geq$5) different research areas. Incomparable to Cameroon (n = 3 RA), Rwanda (n = 3 RA), Sudan (n = 3 RA), Ghana (n = 2 RA), Uganda (n = 4 RA), Zimbabwe (n = 4 RA), Cote Ivoire (n = 2 RA), Democratic Republic of Congo (n = 1 RA), Djibouti (n = 1 RA), Guinea (n = 1 RA), Malawi (n = 1 RA), Mali (n = 1 RA), Senegal (n = 1 RA), Sierra Leone (n = 1 RA), Tanzania (n = 1 RA), Togo (n = 1 RA) and Zambia (n = 1 RA), which are involved in less than five research areas (Figure 5).

Moreover, an analysis of funding agencies and several funding awarded (FA) was conducted (Figure 6). The five most active African countries (Egypt, South Africa, Tunisia, Morocco, and Nigeria) are funded by different funding agencies internationally and domestically. The top funding institution for Egypt is the National Institutes of Health (n = 19 FA), for South Africa, it is the National Research Foundation South Africa (n = 22 FA), and Tunisia's funding agency is the Tunisian Ministry of Higher Education and Scientific Research (n = 3 FA). The top funding agencies that are on a similar scale for the total number of awarded funding for Morocco are Fondazione Umberto Veronesi (n = 2 FA), Groupe Franco Africain D'Oncologie Pediatrique (n = 2 FA), Noujoum Association De Parents Pour Le Soutien Aux Enfants Hospitalises (n = 2 FA) and St Jude Children's Research Hospital (n = 2 FA). While Nigeria is mostly funded by the Alzheimer S Society (n = 4 FA), Medical Research Council UK (n = 4 FA), and UK Research Innovation (n = 4 FA) on a similar scale for the total number of awarded funding. Notably, they are all highly funded by international funding agencies, except South Africa and Tunisia which receive funding from mostly domestic funding agencies. It was also noted that some of the African countries

that are active in neuroblastoma research did not declare the funding agencies, as depicted in Figure 6.

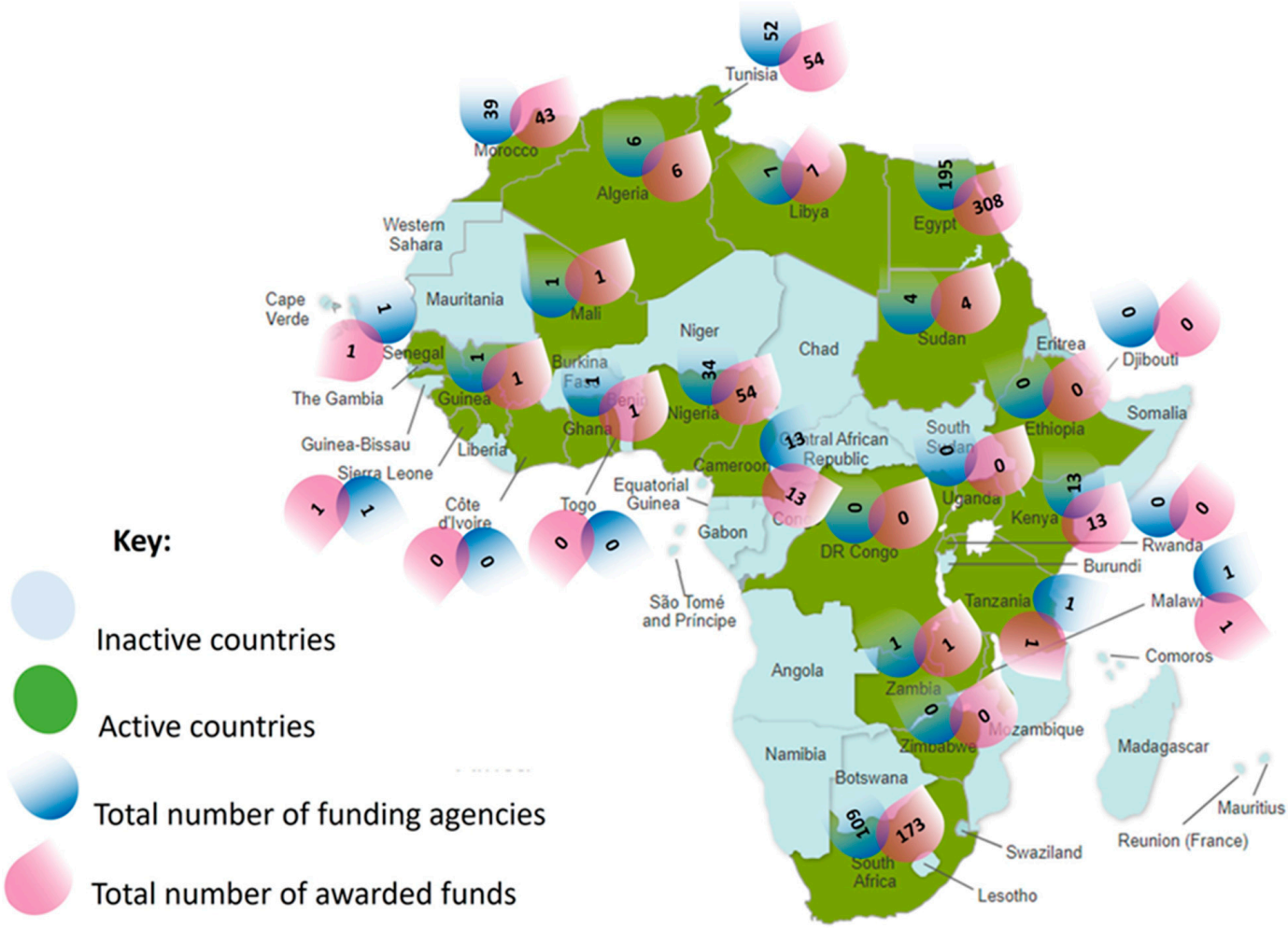


Figure 6. Declared and undeclared funding agencies and awarded funds for neuroblastoma research in active African countries from the year 2000 to 2024.

3.4. Cooperation of African Countries/Regions

The collaboration between different African countries/regions with international countries/regions is demonstrated in Figure 7. The thicker lines amongst countries/regions represented in Figure 7, indicate a higher level of cooperation between the countries. The United States collaborates with most countries, including African countries. In Africa, Egypt, and South Africa are amongst the countries which collaborate the most with other countries.

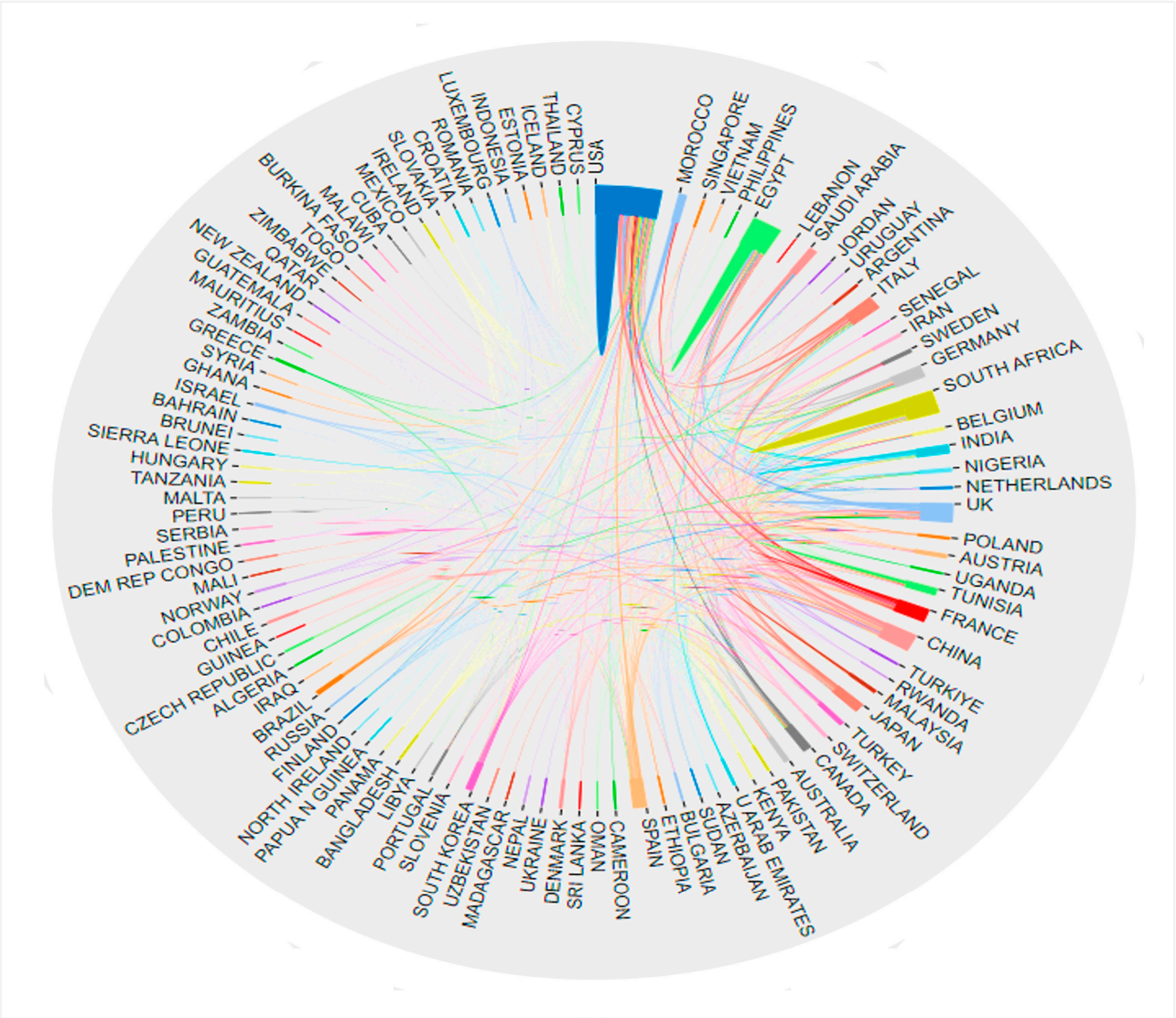
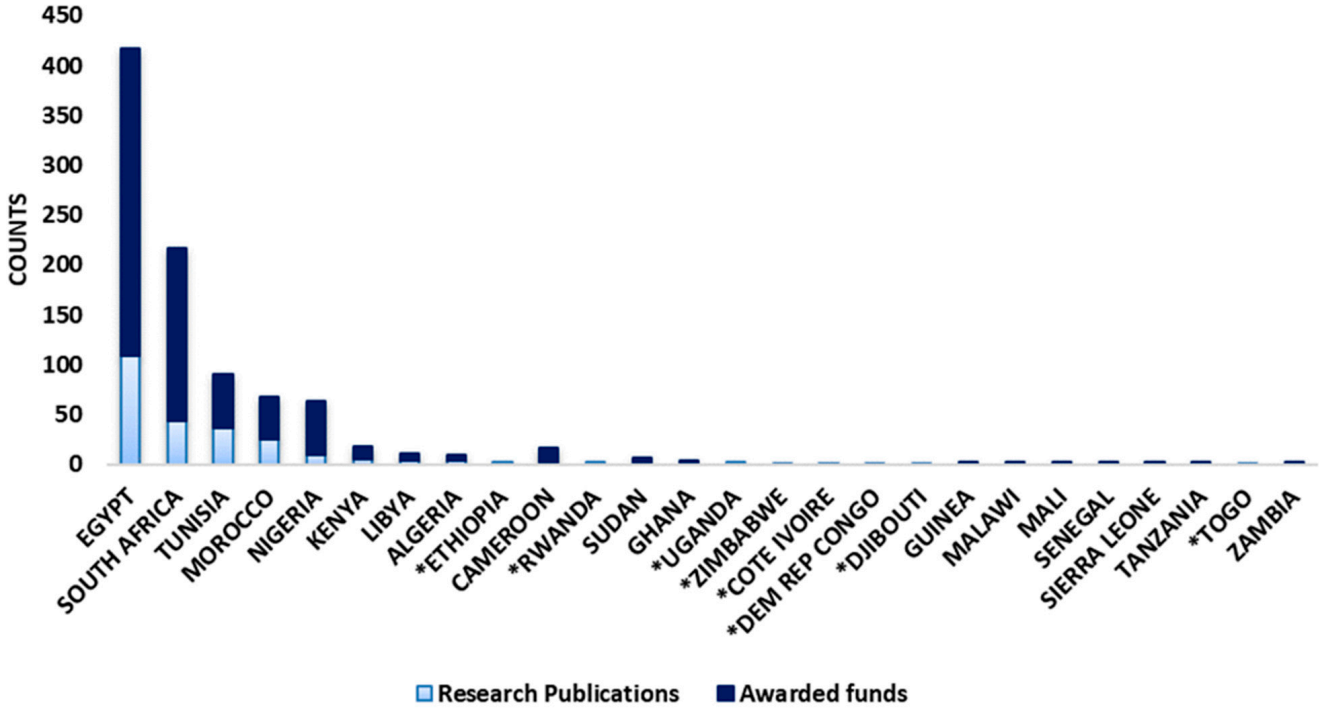


Figure 7. Cooperation analysis among African countries with different international countries which are active in neuroblastoma research field from the year period of 2000 to 2024. Key: The thicker the line the greater the cooperation.

3.5. Correlational Data of African Neuroblastoma Research

Pearson correlation coefficient value (r = 0.9744) represented in Figure 8a, shows that there is a positive correlation with no significant difference (p = 0.131; r^2 = 0.089) between the quantity of research publications and awarded funds in African countries. Moreover, there is a noticeable projected association trend in Figure 8b, between the quantities of research publications and awarded funds per African countries. The top five African countries with high research activity (Egypt, South Africa, Tunisia, Morocco, and Nigeria) are among the countries that are awarded more funding. Although other African countries, specifically Ethiopia, Rwanda, Uganda, Zimbabwe, Cote Ivoire, Democratic Republic of Congo, Djibouti, and Togo did not declare their awarded funding, they still managed to publish (Figure 8b).



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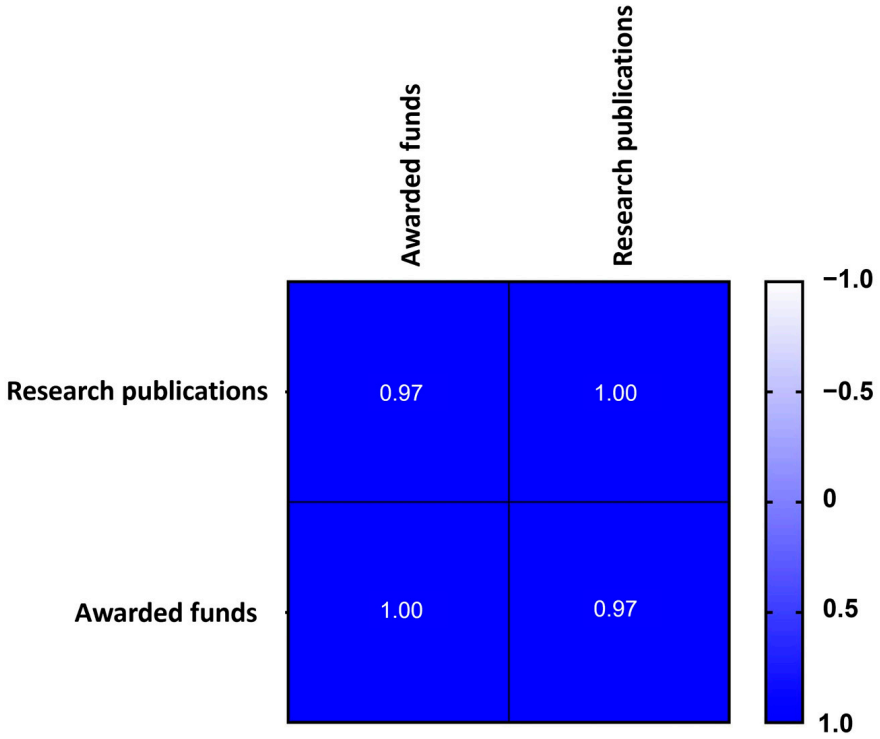

(**b**)

Figure 8. Correlational data of neuroblastoma research Africa: (**a**) Trends of correlations between research publications and awarded funds per African country; (**b**) Pearson correlation of research publications and awarded funds. Key: * No awarded funding.

4. Discussion

The view that Africa has embraced the SDGs framework in conjunction with the 2030 Agenda and 2063 Agenda reveals that the continent is optimistic about reaching the SDGs goal by 2030. African governments have endorsed and incorporated the SDGs into their national plans and actions [103]. However, the ability and competency of many African countries are still partially hindered due to a lack of resources [104]. In this study, African countries focused the neuroblastoma research publications mainly on sustainable development goals of good health and well-being. Moreover, these results also revealed that there is minimal progress and, in some instances, complete stagnation in terms of neuroblastoma research related to other sustainable development goals of zero hunger, gender equality, clean water and sanitation, partnerships for the goals, good health and well-being, reduced inequalities. The SDGs above correlate to neuroblastoma in the following ways:

Zero hunger: Lack of adequate nutrients due to communities being impoverished can affect the health and the quality of life of individuals. This can be detrimental to individuals who already have weakened immune systems due to cancers such as neuroblastoma, making them highly susceptible to other infections. The efficiency of neuroblastoma treatments can also be affected by poor nutrition.

Gender equality: Access to health care should not be discriminatory to females as all individuals should be treated equally. This will ensure that all individuals will receive adequate health care and appropriate treatment on time.

Clean water and sanitation: Good sanitation and clean water ensure reduced probabilities of contracting infections and other illnesses that may further weaken an already debilitated immune system due to neuroblastoma. Additionally, any other infections may hinder the efficacy of the treatment provided to the affected individual.

Partnerships for the Goals: Partnerships between healthcare and scientific institutions as well as governments across the world may achieve more research goals surrounding treatments of neuroblastoma and this may, inadvertently, reduce the mortality rates of neuroblastoma patients

Good health and well-being: Early diagnosis can reduce the mortality rates of neuroblstoma, and this can be achieved by regular screening through promoting good health and well-being. Early treatment can greatly reduce the severe adverse effects of neuroblastoma.

Reduced inequalities: The majority of individuals in low-income countries have limited access to adequate health care due to financial barriers such as the inability to afford high-end treatment for neuroblastoma or due to the lack of transport to hospitals and health care institutions and this is most prevalent in rural areas. This highlights the role of affordability and accessibility in the inequalities between patients of neuroblastoma

In addition, there is a large degree of inevitable involvement of Egypt, South Africa, Tunisia, Morocco, Nigeria, Kenya, Libya, Algeria, and Ethiopia in more than four different research areas. Egypt, South Africa, Algeria, and Nigeria have the highest number of paediatric oncologists of all African countries. South Africa established a neuroblastoma workgroup in 2016 and initiated the development of a treatment protocol and the results formulated a publication in 2019. Countries such as South Africa, with national treatment protocols, report more [105]. The overall dominating research area in Africa is oncology followed by pharmacology. This would be a successful attempt in flagging cognizance to amid policymakers and researchers about the prevalence of neuroblastoma [14]. The World Health Organization's Global Initiative for Childhood Cancer, which collaborates with stakeholders across multiple sectors worldwide has the conjoined goal of increasing survival rates of paediatric cancer patients globally [106]. Established in 2018, the initiative aims to improve the quality of life and to increase the survival rate to 60% by 2030 [106]. The main focus of the initiative is to target six childhood cancers which are, Low-grade glioma (a brain cancer), Burkitt lymphoma (a fast-growing lymph gland cancer), Hodgkin lymphoma (a lymph gland cancer), Wilms tumor (a childhood kidney cancer), Retinoblastoma (a childhood eye cancer), Acute lymphoblastic leukemia (a blood cancer) and through the improvement of these diseases, progress can be made on other childhood

cancers [106]. These developments may swiftly progress to more resources being channeled into neuroblastoma.

There is a needfor an increase in neuroblastoma research from year 2000 to 2024, with disproportionate distribution across Africa reflected in this study. Only 26 of 54 African countries were accountable for total neuroblastoma research in Africa, with South Africa and Egypt contributing 61% of the whole continent's neuroblastoma research. This can be explained by a number of factors which include the fact that both South Africa and Egypt are ranked the first two highest countries in the continent with the highest Gross domestic product (GDP) [107]. Moreover, Egypt and South Africa were statistically documented as the first two African countries with the highest gross domestic expenditure on research and development (GERD) which was 8.86 billion U.S. dollars and 6.2 billion U.S. dollars, respectively in the year 2022 [108]. However, Algeria was ranked the third highest African country in terms of GERD, the results revealed that its continentally contributed only 1% in the neuroblastoma research field.

Nonetheless, as indicated in the current study, Egypt and South Africa are mostly funded by different funding agencies internationally and domestically. The top funding agency for Egypt is the National Institutes of Health based in the USA and for South Africa is National Research Foundation South Africa which is a domestic agency. In general, there is weak federal national funding for neuroblastoma research in African countries, as revealed in this study. While international funding is as equivalently important as national funding, it is also crucial for instituting a maintainable African-based neuroblastoma research setting. In comparison with other African countries, the high share of South African local funding may be explained by the fact that in the year 2003, South African government allotted a new funding system which is based on the tertiary institutions research output [107]. This was dependent on the worldwide expenditure on science and the increasing number of scientists in the previous five years. At least all African countries must spend 1% of their GDP on research and development as recommended by the African Union [109–111]. Even though South Africa is approximately accomplishing this goal, which is also probable, it clarifies its high percentage contribution to African neuroblastoma research.

The collected analyzed data of this study draws special attention to a distinct and enduring upward correlating trajectory of Africa's neuroblastoma publication numbers, their citations, and acquired funds. However, there is still room for improvement in reaching a higher h-index in the neuroblastoma-based field rather than the current attained index of 44 which is far less when compared to other international countries. The shortage of citations may be due to the journal choice for publication. This indicates the necessity of targeting the submission of manuscripts to more journals that are indexed. This can be eased by author availability and receiving fee waivers from indexed journals, since funding is a major drawback among African countries in terms of neuroblastoma research output. Moreover, our results show that in Africa, Egypt, and South Africa are among the countries which collaborate the most with other countries. African neuroblastoma researchers can form more intercontinental collaborations within Africa and, put into consideration a multi-national funding attraction as suggested by Miles et al. [112]. Thus, national cancer control plan goals must also emphases on identifying the current status of cancer research-related resources and its effective utilization. Albeit the challenge we face of national cancer control plans scarcity in Africa [113], which highlights the inadequate national health investment options in cancer care.

Limitations of the Study

Due to the shortage of citations, which may be caused by the choice of journal for publication, appropriate and suitable research can be impacted as quality studies may be under-cited. This, inadvertently, highlights the need to submit manuscripts to journals that are indexed. Various databases have limited access, and this may inevitably restrict access to high-quality and relevant publications. This is, especially, applicable to most African countries that are not highly represented in some scientific databases. Research

from Africa might have not been proportionately distributed across the different countries and important scientific research may have been overlooked especially from countries with low research activity. Neuroblastoma research, specifically, is intertwined with other disciplines such as paediatrics and cancer, therefore extrapolating and analysing conducive information pertaining to Neuroblastoma was challenging. Irrespective of these challenges, this study provides a comprehensive insight into Neuroblastoma in Africa.

5. Conclusions

This heterogeneity finding flags the necessity of developing a comprehensive strategic plan and implementation to cultivate neuroblastoma research as a fundamental part of each African country's national cancer control plan. This strategic plan may also be guided by the following five-point plan in terms of the research category.

Five-Point Plan

- Funding plan: To intensify the visibility of the African continent, neuroblastoma research must be a significant constituent of each national cancer control plan through Africa, allied to hypothesize federal funding. Moreover, African academic and research institutes need to develop independent sources of funding for both federal and philanthropic gestures. This will permit Africans to initiate their particular research agenda which will lead to less reliance on international research funders. Government, researchers and the public in general must engage with the philanthropic sector for significant contributions to neuroblastoma research funding.
- GDP plan: It is important to strengthen African countries' national research provisional streams from governments and private funders. Moreover, African countries have devoted to use 1% of GDP for gross domestic expenditure in research and development. This percentage must not be partially utilized and 10% of this 1% should be allocated to cancer-related research areas. This is prompted by the prevalence, progression and complication of cancer prevention and treatment could be singled out for special consideration.
- Authors and Publications plan: Capacity building of neuroblastoma researchers must be encouraged to publish in trustworthy journals that are indexed, and fee waiver must be provided for low-income African countries. Publishing in such journals for researcher's advancement will add positively to the research output of the African continent. Moreover, researchers must receive financial rewards for excellence in African research outputs as a form of encouragement to further pursue neuroblastoma-based research. An increase in African neuroblastoma research advocacy campaigns is essential for the elevation of African profile research and its significance worldwide.
- Collaboration plan: The pan-African cancer research repository has to reinforce the establishment and implement a different collaborative research model, comprising of capacity building, to improve international, intercontinental, and regional collaborations. In addition, implementation of the development of research through Africa which includes multi-linguistic collaborations that encourage research in Lusophone and Francophone countries of Africa, ensures that all African continents are represented.
- SDGs plan: African universities must also focus on quality research especially at a post-graduate level of Masters and Doctorate stages, combined with the economic impact of research and accomplishing sustainable development goals.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/publications12040045/s1. Table S1: World Bank Country and Lending Groups. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.

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