Evidence for decreasing sperm count in African population from 1965 to 2015

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Abstract

Purpose: This meta-analysis, following our previous reports those documented an overall 57% diminution in mean sperm concentration around the globe over past 35 years and 32.5% decline in past 50 years in European population, attempts to report the declining trend of sperm concentrations in African population between 1965 and 2015.

Methods: In the course of retrieval of data following MOOSE guidelines and PRISMA checklist, we found a total of fourteen studies that have been conducted during that period on altering sperm concentration in the African male.

Results: Following analysis of the data, a time-dependent decline of sperm concentration ($r = -0.597$, $p = 0.02$) and an overall 72.6% decrease in mean sperm concentration was noted in the past 50 years. The major matter of concern is the present mean concentration (20.38×10^6/ml) is very near to WHO cut-off value of 2010 of 15×10^6/ml. Several epidemic diseases, genital tract infection, pesticides and heavy metal toxicity, regular consumption of tobacco and alcohol are reported as predominant causative factors.

Conclusion: This comprehensive, evidence-based meta-analysis and systematic review concisely presents the evidence of decreased sperm concentration in the African male over past 50 years with possible causative factors to serve the scientific research zone related to male reproductive health.

Keywords: Semen quality, sperm concentration, sperm count.

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Introduction

A worldwide decline in sperm count has been presented vastly in past few decades through several studies[1,2]. The deterioration of semen quality was first noted in 1974 by Nelson and Bunge[3]. In 1992, Carlsen et al. reported a global decline in sperm counts in a meta-analysis of 61 studies between 1938 and 1990 evaluating the semen analyses of 14,947 presumably fertile men from 23 countries[4]. In that analysis, they have found significant declines in sperm count in the United States, Europe, and Australia, but no such decline in non-Western countries. Similar declines were also proclaimed by numerous other studies, but were unable to establish a clear cause[5,6] But, since then the reports published regarding the changes in human semen parameters were so far inconsistent: Nieschlag et al.[7] reported no changes in any parameter[7], while Ng et al.[8] revealed significantly different seminal volumes in different age groups[8]. Recently, Rolland et al.[9] in their analysis showed 32% decline in sperm count from 1989 to 2005[9]. In our recent articles, we have also reported decline in semen volume[10] and sperm count[11] in males over past few decades.

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Reports regarding the altered sperm concentration in African sub-continent is very limited. The first document regarding altered sperm concentration of the African population after 1965 was put forward by Chukudebelu et al.[12]. But during 1965-1979, there is no study recounting altering sperm concentration in Africa. But, there are plenty of articles which report causes and risk factors of male infertility in the African population. These reports showed that significantly increased serum follicle stimulating hormone (FSH)[13] and decreased inhibin B[14] may result in testicular spermatogenic dysfunction[15]. Changes in sperm count can also occur after occupational and environmental exposure to toxic agents[16-19] or from the predisposing factors of the host, such as age[20-22].

Thus, the objective of this meta-analysis was to build-up a substantial idea regarding alterations in sperm concentration in the African population by picking the scattered reports of past 50 years, moulding them in sequential pattern, statistically analysing and through the systematic review looking over the linking factors of decreased sperm concentration.

Data extraction and data anaysis

Research articles on humans published in English from 1965 to 2015 were included in this report[23-36] (Table 1).

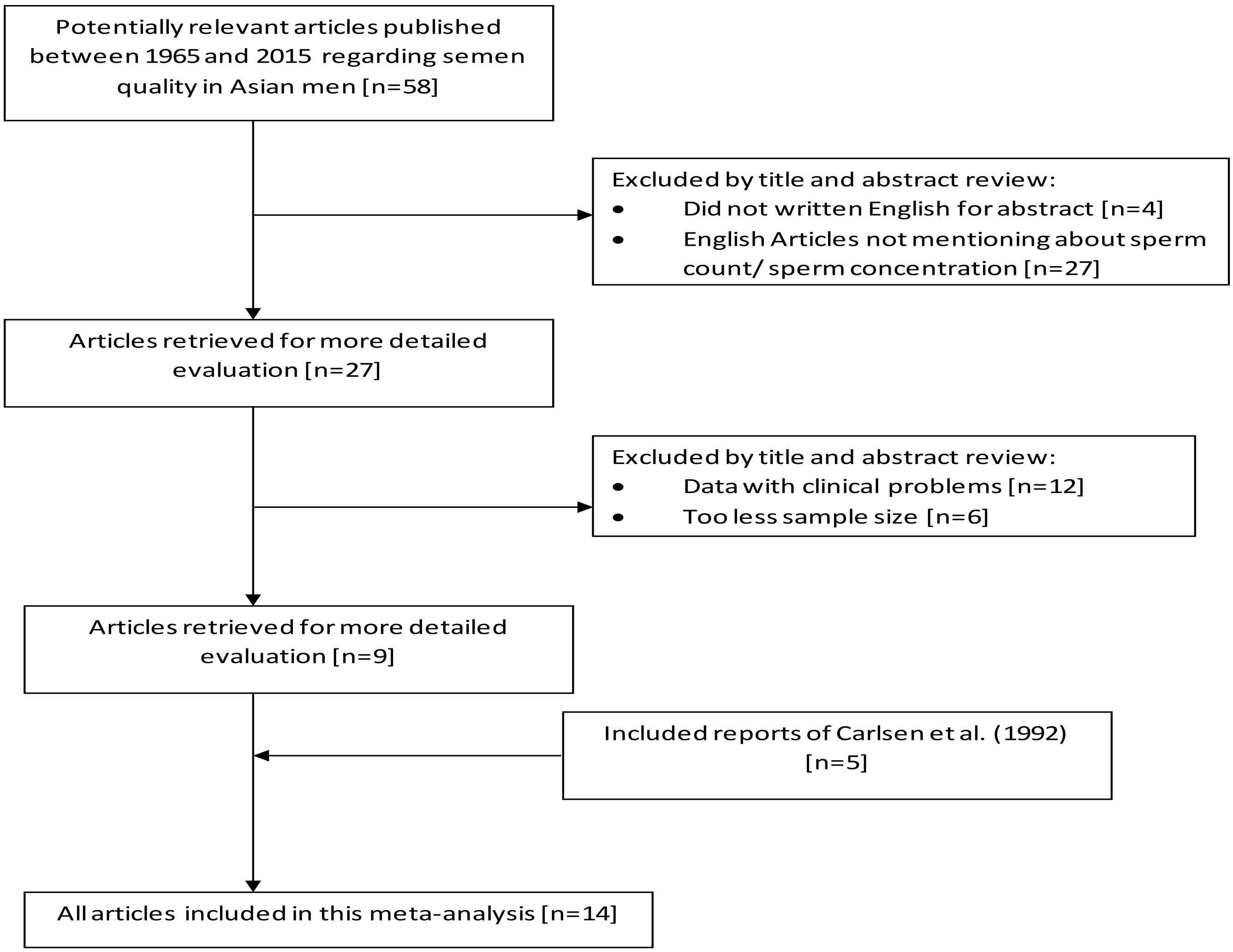
Table 1. Studies on changes of sperm concentrations in different age groups in past 50 years in Africa.

Country	Population	Sample size (n)	Male age definition (range/ mean/ group, in years)	Direction of effect with increasing age	Study
Nigeria	Cohort study	53	20-45	↓ (P<0.01)	Lapido, 1980
Egypt	Andrology lab	45	19-53	↓ (P<0.01)	Shaarawy and Mahmoud, 1982
Libya	Infertility clinic	1500	20-45	↓ (P<0.01)	Sheriff, 1983
Nigeria	Cohort study	100	20-45	↓ (P<0.01)	Osegbe *et al.*, 1986
Libya	Cohort study	10	No age data	↓ (P<0.01)	Sheriff, 1987
Tanzania	Andrology lab	120	19-55	↓ (P<0.01)	Kirei, 1987
Nigeria	Cohort study	20	19-53	↓(P<0.001)	Sobowale & Akiwumi, 1989
Nigeria	Andrology lab	21	19-24	↓ (P<0.05)	Nnatu *et al.*, 1991
Libya	Cohort study	1250	19-53	↓ (P<0.01)	Sheriff and Legnain, 1992
Nigeria	Infertility clinic	170	25-40	↓ (P<0.001)	Ugwuja *et al.*, 2008
Tunisia	Infertility clinic	2940	20-45	↓ (P<0.001)	Feki *et al.*, 2009
Nigeria	Cohort study	106	20-45	↓ (P<0.01)	Akande *et al.*, 2011
Nigeria	Infertility clinic	316	20-40	↓ (P<0.05)	Jimoh *et al.*, 2012
Tunisia	Andrology lab	116	Males of mean age 32.74	↔ (NS)	Hadjkacem Loukil *et al.*,2015

Data are represented as Mean(SD); ↓=decrease; ↑=increase; ↔ = no change; NS=not significant at P<0.05, no *P* value indicates that no statistical testing was done

We also included the reports of Carlsen et al. (1992), i.e. reports from 1965 to 1992[4]. We selected publications about sperm concentration, with pre-defined criteria for inclusion and exclusion, as follows. [1] The non-Carlsen studies published during 1965 to 2015 were identified by using Medical Subject Headings (MeSH) of electronic databases which included Medline, National Library of Medicine, Bathesda, MD with the key words: sperm count, sperm density, sperm concentration, semen quality, male infertility and semen analysis. [2] Relevant literature on changes of the sperm concentration and its influence on future natural and assisted conception cycles were retrieved. [3] Data of the subjects with clinical problems were excluded. [4] Studies with insufficient numbers of subjects (n < 5) were excluded. We followed Meta-analyses of Observational Studies in Epidemiology (MOOSE) guidelines[37] and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist[38], 2009 to extract the data using the above mentioned electronic databases (Table 2). In each case sperm concentration and its outcome were evaluated. Analytic epidemiological studies were emphasized. Therefore, the current analysis was based on 14 African studies published in 1965-2015. For simple statistical analyses Microsoft Excel v.2013 was used and correlation and regression analyses of data were done using StatSoft. (2011) and SPSS v.22.0 to calculate correlation coefficient and it was considered to be significant if p was <0.05 or <0.001[39]. Mean sperm concentrations of all 14 reports were also analyzed with linear regression weighted by number of subjects included in the individual publications.

Table 2. Flow chart of study selection according to MOOSE guidelines.



State of affairs: past 50 years

African scenario

In 1991, WHO had estimated that almost 20-35 million couples were infertile in Africa[40]. Nigeria is suggested to have been suffering from highest infertility problems among the other African regions, the male infertility factor accounting for 40-50%. The degree of infertility and its cause vary from place to place. These are evident from the study pursued in mid-Western Nigeria which brought to the lime light that about 50%, of the 780 couples under evaluation, differed in the causes of their infertility[41]. Study associated with South-Western Nigeria reported that 42.4% infertility resulted from the male factor[42].

During the retrieval of relevant documents, we found only fourteen studies which had been conducted on alterations of sperm concentration of African population in the last 50 years. The outcome of these studies is represented in Table 1. Most of the reports were based on epidemiological studies (43%), and others included andrology laboratories (29%) and infertility clinics (29%). Among the 14 published research works discussed in this article from 1965 to 2015, most were carried out in Nigeria. Most of the studies used sample size less than 500 men (79%) and only three studies included sample size >1000 (21.43%). Out of 14 reports, 93% have provided data about the age of subjects; all of these reports depicted significant decrease in sperm concentration from 1965 to 2015 while only one report showed no significant alteration. We also recorded that most of the studies were carried out in Nigeria. A time-dependent decline in sperm concentration was observed from 1965 to 2015 ($r = -0.597$, $p = 0.02$; Fig 1) that reflected an overall 73% decrease in sperm concentration (Fig 2).

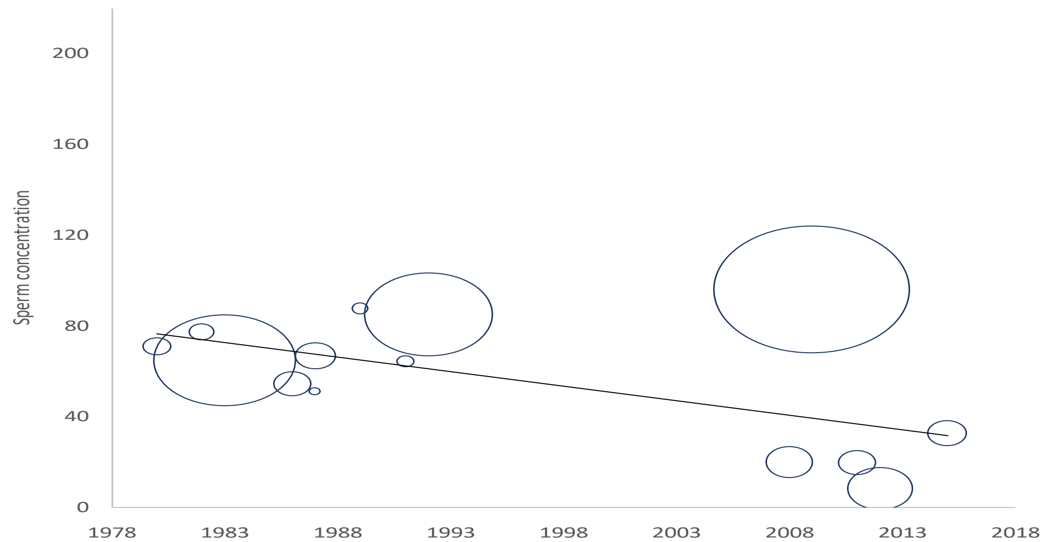


Fig 1. Temporal decline in sperm concentration (×10^6/ml), bubble size corresponds to the number of men in study following Table 1

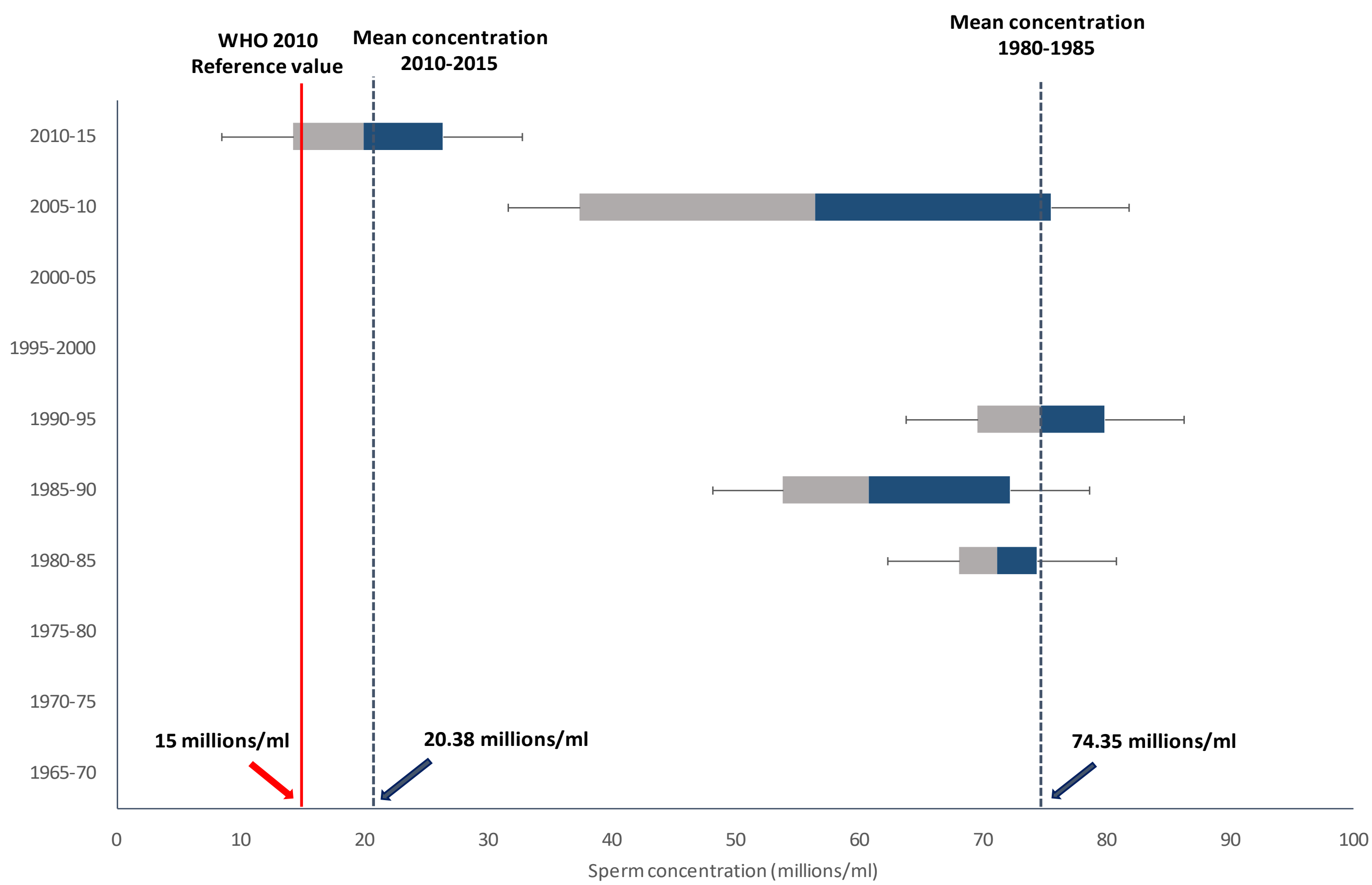


Fig 2. Box and whisker plot of sperm concentration data of African men between 1965 and 2015 with WHO cut-off value (2010).

It is thus understandable that regional variations in reproductive status prevails in Africa and the high rates of male infertility in Nigeria is thought to be due to infections, sexually transmitted diseases and hormonal abnormalities[43,44]. But, the major matter of concern is that the present mean concentration (20.38×10^6/ml) is very near to WHO cut-off value of 2010 of 15×10^6/ml.[40]

Comparing with global scenario

In one of our recently published article, we showed a significant decrease in sperm concentration worldwide between 1980 and 2015 from 91.65×10^6/ml to 39.34×10^6/ml ($r = -0.313$, $p = 0.0002$). It reflected almost 57% decline in sperm count worldwide from 1980. It also showed that recruitment of larger population for this type of study increased predominantly after 1995[11]. In another report, we revealed a time-dependent decline of sperm concentration ($r = -0.307$, $p = 0.02$) in European men from 1965 to 2015 and an overall 32.5% decrease in mean concentration[45].

Recent studies on male reproductive system when brought together bring conflicting evidence to the forefront regarding sperm counts with some showing significant decline while some found no change. North America, Europe and Asia were more prone to a declining trend of sperm counts over the years whereas studies based on South America and Australia do not depict such a trend[11]. However, in this present analysis a significant decline in sperm concentration has been noted in the African population. It has been suggested that these regional differences in sperm counts possibly are biologically meaningful. Most of the controversies that aroused from the past clinical studies about semen quality may be partly due to involvement of only few selected groups of men. In many studies, historical data collected for other purposes has been used without close attention to important and specific factors relevant to an analysis of secular or geographical trends.

Possible causative factors

Although little is known about the causative factors for the decline in sperm count worldwide, significant associations have been reported between impaired semen quality including sperm count, and several of the etiological factors in developing countries especially Africa[46]. We also reported some link factors of declining sperm concentration worldwide[11], but the proper correlation with a single factor is difficult to establish.

In Africa, it has been reported that some epidemic diseases, like malaria, Schistosomiasis and viral infections play pivotal roles in the declining sperm concentration[47,48]. Yeboah et al. in 1992 reported that in Ghana they found a 12% higher incidence of inflammatory testicular or prostatic conditions as compared with those found in Europeans, suggesting that inflammatory conditions contribute more to male infertility and declining sperm concentrations in Africa.[47] Genital tract infections and sexually transmitted infections are associated with declining sperm concentrations in African men[49,50]. Okonofua et al. found that infertile and sub-fertile men are more likely than fertile men to report having experienced penile discharge, painful micturition and genital ulcers, yet they are less likely to present to a formal health institution to seek treatment.[50] Therefore, poor health-seeking behaviour of our African men is key to the declining sperm concentration[41,50].

Regular alcohol consumption and tobacco smoking are responsible for the declining sperm concentration[50]. Several studies reported that these two factors are the principal causes of hypogonadism and could cause testicular failure[51]. Therefore, it is possible that the increased consumption of alcohol and tobacco smoking could be a contributory factor to the global fertility crisis in the human species[52]. Moreover, tobacco smoking increases intake of cadmium, because the tobacco plant absorbs the metal. Cadmium, being chemically similar to zinc, may replace zinc in the DNA polymerase, which plays a critical role in sperm production[53]. Geographic differences in the amount of naturally occurring cadmium have been correlated with incidence rates of prostate cancer[54]. Major changes in the levels of toxic elements in seminal fluid have been related to abnormal spermatozoa function and fertilizing capacity[55]. Cadmium has beendetected in significantly high levels in serum of men who were smokers and thus implicated this metal as one of the causes of asthenoteratozoospermia[55].

Cigarette smoking is an important variable when considering the effect of both lead and cadmium exposure on human health. A single cigarette has been reported to contain 1.5μg of cadmium. Moreover, one tenth of the metal content of a cigarette is inhaled[56]. Unlike in most developed nations, there are no smoking restrictions in Africa. Even where there are, they are not obeyed. Cumulative evidence suggests that cigarette smoking has a deleterious effect on male fertility by reducing sperm production, motility, and increasing the number of abnormal sperm[57]. Smokers are 60% more likely to be infertile compared to non-smokers. Cigarette smokers were also shown to have higher levels of circulating estradiol and decreased levels of LH, FSH, and prolactin compared to non-smokers, all of these negatively impact spermatogenesis[57].

Emokpae et al. in Kano, Nigeria reported that endocrine abnormalities are common in the infertile males[58]. Hormonal abnormalities were detected in 22% of oligospermic, 40.7% of severe oligospermic, and 43 of azoospermic subjects. Similarly, hormonal imbalance was also found by Ozoemena et al. in Enugu to be significantly associated with declining sperm concentration and male infertility[59]. They demonstrated that as much as 80.1% of their subjects were found to have a hormonal imbalance and recommended that hormonal profile should be considered as the gold standard for diagnosis and management of male infertility. An observational retrospective study conducted on 1,201 men (mean age of 35.7 years) in Northern Nigeria investigated for infertility at University of Maiduguri Teaching Hospital, over a two-year period, (2004-2006) showed that 96 (7.9%), underwent hormonal assessment because of abnormalities of their sperm counts. 68 (71%) patients had primary infertility and 72 (75%) had azoospermia. 88 (92%) patients had abnormal hormonal assays, giving a prevalence of endocrine abnormality of 7.3%[60].
Therefore, endocrinopathy is also common among infertile Nigerian men as with their counterparts elsewhere. However, the prevalence of endocrinopathy of 7.3% was lower than that reported from Kenya[61], an African country, but higher than that reported in Brazil a developing country like Nigeria[62].

Numerous anti-oxidant nutrients such as vitamin C, vitamin E, glutathione and co-enzyme Q10 have been documented in several studies as having modulatory effects on sperm parameters[52,63]. These positive effects may not be observed in Africa because of the well-recognised deficiency of protective micronutrients in this region[64]. Studies have shown that the concentration of ascorbic acid in seminal plasma directly reflects dietary intake, and lower levels of vitamin C may lead to infertility and increased damage to the sperm genetic material[65]. Ebesunun et al. determined ascorbate levels in the plasma of 27 Nigerian males with inadequate spermatogenesis[66]. There were significant decreases in the seminal and plasma ascorbic acid concentration in males who had inadequate spermatogenesis compared with the control values and the author concluded that semen ascorbate levels may play a significant role in reduced sperm characteristics in these patients[52,66]. Selenium and glutathione are essential to the formation of phospholipid glutathione peroxidase, an enzyme present in spermatids, which becomes a structural protein comprising over 50% of the mitochondrial capsule in the midpiece of mature spermatozoa. Deficiencies of either substance can lead to instability of the midpiece, resulting in defective motility[52,63]. Akinloye et al. in their study observed a significant inverse correlation between serum selenium level and sperm count. Similarly, seminal plasma selenium correlated with spermatozoa motility, viability, and morphology[67].

The spermatotoxic effects of dibromochloropropane (DBCP), a nematocide widely used in agriculture was reported in the early 1960s in rodents by animal toxicologist but their report went essentially unnoticed until the late 1970s when oligospermia and azoospermia were reported in manufacturing plant workers and pesticides applicators[68]. It was noted that there was limited childbearing among the workers after they started working in DBCP production. About half of the DBCP-exposed azoospermic men remained that way for many years suggesting that all of the stem spermatogonia may have been compromised. 71 others experienced a recovery in their sperm count, but in some cases the recovery did not occur until 3 to 6 years later[68]. Furthermore, the men had high levels of FSH and LH in serum indicating that DBCP action is directly on the Leydig cells causing alterations in androgen production and action[68]. Other pesticides such as dichloro-diphenyl-trichloroethane (DDT), endosulphan, and organophosphorus pesticides i.e. malathion, have been reported to show male-mediated adverse reproductive outcomes such as abortions, stillbirths, congenital defects etc. among occupationally exposed workers[69].
A significantly higher level of asthenozoospermia and teratozoospermia was found in 2, 4-dichlorophenoxy acetic acid exposed workers as compared to unexposed control subjects[70]. Although DDT production has been banned in the United States for more than 2 decades, new factories are still being built to produce in some developing nation. The presence of these chemicals in some developing countries is of concern since they are probably accumulating to harmful levels. Ibeh et al. reported higher concentrations of aflatoxin B1 (AFB1) in the semen of infertile Nigerian men than those levels in fertile controls and concluded that the consumption of AFB1 contaminated diets may predispose to male infertility in Nigeria[71]. Over five billion people in developing countries worldwide are at risk of chronic exposure to AFB1 through

food products contaminated by the fungal moulds. The infertile men with aflatoxin in their semen showed a higher percentage of spermatozoa abnormalities (50%) than the fertile men (10-15%). The above observations therefore suggest that pesticides, industrial chemicals and mycotoxins like aflatoxins might be implicated in the declining fertility of the African men[71].

A number of occupations are being reported as risk factors for male infertility. For example, an insult to spermatogenesis has been reported among professional drivers who are exposed to the products of fuel combustion, noise, vibration, emotional stress, physical load on the pelvic organs and increased temperature in the pelvis because of prolonged sitting[72]. Intense exposure to heat in the workplace e.g. working in furnaces or in bakeries, long soaks in the bath tub, use of laptops, and excessive bicycling can cause the temperature in the scrotum to increase enough to impair sperm production. Welders are also at risk due to their exposure to heat, solvents, heavy metals and noise[72]. Men who wear tight pants which hold the testes close to the body also vulnerable to these defects[73]. Noticeable improvement in sperm count has been observed when the tight underwear is discarded.

Conclusion

The current meta-analysis, with pertinent evidence reports an overall 73% decline in sperm concentration in African men over past 50 years and the current concentration is very near to WHO cut-off value of 2010 which is a major issue of concern. It also explains the major possible causes of the declining trend. Poorly treated sexually transmitted infections (STIs) and hormonal abnormalities, consumption of excessive alcohol and tobacco smoking are reported as the major causes. But, according to the published articles describing the link factors of male infertility in Africa, exposure to pesticides and heavy metals are the principal triggers of decreased sperm concentration. However, as more than one factor is involved in this decreasing trend, correlation with a single factor is difficult to establish. Conceivably in future with the development of more sensitive biomarkers, we will be able to relate these factors with decreasing sperm concentration precisely.

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Conflict of interest

None

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