Histological and Functional Effect of Aluminium on Male Reproductive System

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Abstract

Various findings are given emphasis to Aluminium which has more and more obvious disturbance of the reproductive processes other body organs. The purpose of this review is to give a comprehensive report of the existing data on Aluminium induced male reproductive toxicity in different animal models. Along with, we also have made an attempt to present the possible mechanism related to Aluminium induced reproductive toxicity suggested by various researchers. The findings showed that Aluminium is one of the ubiquitous metals and is being immensely used in industries, pharmaceuticals, food additives and consumer products. Alongside, there has been an increased incidence of exposure to the general population which can cause serious effect on various systems of the body including male reproductive system. The present analysis indicates that increase oxidative stress, alteration in spermatogenesis as well as membrane function, disruption in cell signaling and the impairment of blood testis barrier, affect the endocrine system which might be the various possible mechanisms of Al induced male reproductive toxicity.

Key words: Aluminium, Male Reproductive System, oxidative stress, Blood Test Barrier, Histological change

Literature search method

I carried out an extensive literature review, including published materials from databases like google scholar, pubmed, hinari and Scopus. Selected papers date between 1980 and 2014. The search methodology can be summarized as follows: after selecting a set of search terms and generating reliable combinations, I used electronic research databases to search for related articles. I then selected a maximum of 58 papers for each combination of search terms. A backward/forward search was conducted, and the abstract was analysed to ensure that the papers met the search criteria. Papers that failed to meet any of the search criteria were excluded.

Multiple combinations were selected using these key search terms, For instance, all possible combinations of Aluminium and oxidative stress; Impairment of blood testis barrier and hitological alternations. These terms were then used on the online databases google scholar, pubmed, hinari and Scopus. Of this initial selection, an abstract matching and backward/forward search was conducted to assess whether the topic covered was relevant.

The search method applied in this review

Step Search method

1. Identify common search terms from reviews, books and technical papers.
2. Generate plausible combinations of terms to be used for search using the key search terms identified.
3. Search for these terms on google scholar, pubmed and hinari and Scopus.
4. Select a base set for the results consisting of the 58 papers
5. Match the abstract and perform a forward and backward search to verify the relevance of the paper for the selected base set.
6. Exclude papers that address none of the topics covered, that only make a brief reference to the subject at hand or that are not written in English.

Introduction

Humans are inexorably out to metals attributable to their ubiquity in nature, polluted air, water, soil and food, wide use in industry and long-term persistence in the environment. Metals may have serious effect on the male reproductive system directly, when they target specific reproductive organs, or indirectly, when they act on the neuroendocrine system. Metals have been shown to affect spermatogenesis in rodents and humans, which can lead to low sperm count, abnormal sperm morphology and poor semen quality [1, 2]. Among them Aluminum (Al) is the most widely distributed trivalent cation found in its ionic form in most kinds of animal and plant tissues and in natural water everywhere. It is the third most prevalent element and the most abundant metal in the earth's crust, representing approximately 8% of total mineral components [3]. Al occurs naturally in the environment and is also released due to anthropogenic activities such as mining and industrial uses, in the production of Aluminium metal and other forms of Al compounds. A variety of Al compounds are produced and used for different purposes, such as in water treatment, papermaking, fire retardant, fillers, food additives, colors

and pharmaceuticals. Al metal mainly in the form of alloys with other metals has many uses including in consumer appliances, food packaging and cookware [4, 5].

Previously Aluminium has been considered on an indifferent element from a toxicological point of view for a long time. Although Al is present in trace amounts in the biological material, it does not appear to be an essential element and is usually considered to have harmful effects on general health [3]. Aluminium is known as a neurotoxin that can cause certain diseases such as Alzheimer disease, dialysis dementia, Parkinsonism, and amyotropic lateral sclerosis In addition[6,7]to its neurotoxicity, Al affects other body structures like the skeletal system [8], brain tissue, bone, blood cells, liver and kidney [8,9]. The sources of Al are specially corn, yellow cheese, salt, herbs, spices, tea, cosmetics, Aluminium ware and containers. Also, Al is widely used in antacid drugs, as well as in food additives and toothpaste [1]. Environmental pollution with the different Aluminium containing compounds, especially those in industrial waste water, exposes people to higher than normal levels of Al [10]. The studies about Aluminium reproductive toxicity are generally poor. Here, we review different scientific literatures to evaluate the functional and histological effect of Aluminium on male reproductive system and its possible mechanism of toxicity.

Effect of Aluminium exposure on male reproductive system

Various studies demonstrated that Aluminum has possible to induce toxic effects in humans or laboratory animals exposed through inhalation, oral, or dermal exposure. It is widely accepted that nervous system is the most sensitive target of aluminum toxicity and it may induce cognitive deficiency and dementia when it enters the brain. Besides this Aluminium ingestion in excessive amount leads to accumulation in target organs and has been associated with damage of testicular tissues of both humans and animals. High Aluminium contents in human testes, Leydig cells, spermatozoa, seminal plasma, blood and urine, were associated with impaired sperm quality and viability [11, 12, 13]. Alteration in the histology of testis [46, 54] deterioration in spermatogenesis and sperm quality; enhancement of freeradicals and alterations in antioxidant enzymes [20, 22, 24]; interruption in sex hormone secretion [21] are several of the aspects suggested that Aluminium exposure causes adverse impact on male reproduction. Table-1 summarizes the observations of aluminium induced male reproductive toxicity in various laboratory animals.

Table - 1 :- Aluminium induced male reproductive toxicity in various laboratory animals

No.	Animal model	Route of administration	Dose	Duration	Observations	Reference
1.	Male Wistar rats	Oral Intubation	aluminium chloride (475mg/Kg; 950mg/kg; 1,425mg/kg 1,900mg/kg).	Eight weeks	seminiferous tubules achieve morphological change, vacuolar cytoplasm with loss of normal distribution of the epithelial linning	[54]
2.	Male Wistar rats	Oral Intubation	aluminium chloride (475mg/Kg; 950mg/kg; 1,425mg/kg 1,900mg/kg).	Eight weeks	decrease in sperm count	[55]
3.	Male Wistar rats	Oral Intubation	100 mg AlCl 3 /kg BW	8 weeks	decreased plasma testosterone, sperm count, motility, morphology and viability, SOD	[57]

4.	Male albino rats	Gavage	AlCl 3 (20 mg/kg bw)	70 consecutive days.	decrease in body weight gain, sex organs relative weight, sperm concentration, motility and viability, serum testosterone concentration and superoxide dismutase (SOD) activity while significant increase in sperm abnormalities and TBARS concentrations. Histological structure of the testis showed congestion of interstitial blood vessel, marked degeneration and necrosis of germ cells lining seminiferous tubules, interstitial odema, complete absence of germ cells.	[32]
5.	Male rats	Oral Intubation	AlCl 3 100 mg. / kg. b.wt	90 days	Affects seminiferous tubules and vascular degeneration of the spermatogenic and sertoli cells.	[14]
6.	Male rats	Orally	AlCl 3 (34 mg /kg bw)	70 days	Decrease in weight of testes, seminal vesicle and epididymis as well as sperm concentration, motility, testosterone level, dead, abnormal sperm and testes TBARS concentrations were increased. Histopathological examinations revealed marked lesions in seminiferous tubules.	[24]
7.	Male albino rats	Intra peritoneal injection	15 and 30 mg. / kg. body weight	Five weeks	Low dose showed vacuolar degenerative changes appeared in the cytoplasm of the spermatogenic epithelium and in the Sertoli cells and abnormal distribution of spermatozoa in the Lumina. High dose showed more exaggerated features of focal areas of spermatogenesis, arrest at the spermatid level, degenerative changes in the germinal cells together with few fragmented sperms in the lumen. EM shows primary spermatocytes were clearly affected. At high dose spermatogonia of both types A and B are more affected; spermatocytes and spermatids showed clear degeneration changes; spermatozoa are absent.	[45]
8.	Male albino rats	Intra peritoneally	Al (5 mg/kg body weight)		The germinal epithelium of the seminiferous tubules was thinner in places and spermatids were almost absent; no sperm in the lumen. Electron microscopic study showed irregularities in the nuclear membrane, some damaged mitochondria, a decrease in the number of ribosomes, and an increase in the number of lysosomes in the sertoli cell cytoplasm. An increase in the rough endoplasmic reticulum in the primary spermatocyte cytoplasm. Vitamin E antagonizes the toxic effects of Al at the histological level,	[46]
9.	Rabbit	incubated	Aluminiu	0, 2 and	Percentage of motile and viable sperm	[20]

	sperm	with different concentrations of AlCl(3)	m chloride (AlCl3) 0, 1, 5, 10, 15 and 20 mM	4 hours	decreased significantly. Significant increase in TBARS levels and inhibition in the activities of SOD.	
10.	CD-1 adult male mice	Intra peritoneally	7 or 35 mg Al/kg body weight/day	14 days	Significantly induced higher Al concentrations in serum, testis and epididymis tissue.	[47]
11.	Male mice	Orally	NaF, 10 mg/kg bw/day) and AlCl3, 200 mg/kg bw/day	30 days	Marked histological changes in the epididymis, decreased levels of protein and sialic acid and lowered activities of adenosine triphosphatase (ATPase) and succinate dehydrogenase (SDH) in caput and cauda epididymides, alteration of sperm maturation in mice.	[52]
12.	Male New Zealand white rabbits	Orally	34 mg AlCl3 /kg BW,	Every other day for 16 weeks.	Significantly decreased libido, ejaculate volume, sperm concentration, sperm motility (%) and viability. Live body weight, feed intake and relative weights of testes and epididymis were significantly decreased. Concentrations of thiobarbituric acid-reactive substances (TBARS) were significantly increased.	[22]
13.	Male mice	Drinking tap water	aluminum chloride 1000 ppm (1000 mg/L), 1200 ppm (1200 mg/L) and 1400 ppm (1400mg/L).	12 weeks	Significantly reduced testicular and epididymal sperm counts and increase in testosterone and luteinizing hormone (LH) serum levels. Also, absolute weight of the testes, absolute and relative weights of the seminal vesicles and preputial glands were significantly reduced. Furthermore, histological changes were found in testicular sections of adult male mice ingested aluminium chloride. Congested blood vessels, increased amount of interstitial connective tissue and destruction of the seminiferous tubules with large necrotic areas and degenerative cells have been observed.	[56]
14.	Male mice	Intra peritoneal	Al chloride (0, 1/8 and 1/3 LD(50))	12 or 16 days	Serum testosterone concentrations were markedly decreased. In addition, significant increases in nitric oxide products.	[36]
15.	Adult male mice	Intra peritoneal	aluminum nitrate (0, 50, 100, and 200 mg/kg/day	4 weeks	Decreased testicular and epididymal weights, as well as significant decreases in testicular and spermatid counts and epididymal sperm counts. Histological changes, including necrosis of spermatocytes/ spermatids,	[19]
16.	Male rats	oral intubation	80 mg/kg aluminiu	60 days	significant reduction in sperm counts and the percentage of live sperm, with a	[58]

m chloride	significant increased in the percentage of morphologically abnormal sperm, and a significant reduction in averages of body weights, head epididymis, testis and prostate gland weights in rats treated with aluminium chloride at dose

Possible mechanism of Aluminium toxicity on male reproductive system

Experimental studies suggested that following mechanisms might be committed for the male reproductive toxicity of Aluminium: Increased oxidative stress; Impairment of blood testis barrier and hitological alternations.

Aluminium and oxidative stress

Aluminum is considered to be a non-redox active metal, which promotes biological oxidation both in vitro and in vivo because of its pro-oxidant activity [23]. Testicular oxidative stress appears to be a common feature in much of what underlies male infertility, [23, 24, 56]. The role of oxidative stress in neuronal degeneration is a widely discussed concept, and understanding on the role of Al in mediating testicular toxicity may help to clarify the role of Al in male reproductive damage. Aluminum is a trivalent cation that does not undergo redox changes.

Oxidative stress is an imbalance between free radical generation and the antioxidant defense system. Oxidative stress induced by Aluminium is one of the major contributing factors to male reproductive disorders. Disruption of metal ion homeostasis may lead to oxidative stress, a state where increased formation of reactive oxygen species (ROS) overwhelms body antioxidant protection and subsequently induces DNA damage, lipid peroxidation, protein modification and other effects [25,26]. Despite the low oxygen tensions that characterize the testicular microenvironment, testis remains vulnerable to oxidative stress due to the abundance of highly unsaturated fatty acids (27).

Testosterone is a key hormone that regulates spermatogenesis. Environmental contaminants are known to induce reproductive toxicity by disturbing the pro-oxidant and antioxidant balance leading to oxidative stress [28]. In the study of Arumugam Kalaiselvi *et al*, Aluminium chloride treatment decreased the activities of antioxidant enzymes like superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and glucose-stransferase [27]. The reduction in the activities of antioxidant enzymes could reflect the adverse effect of Aluminium chloride on antioxidant system in the testis and the epididymis of rats. Aluminium induced significant decrease in serum testosterone concentration and SOD activity, with significant increase in TBARS levels compared to control rats [29, 57]. SOD is considered as the first line of defense against deleterious effects of oxyradicals in the cell by catalyzing the dismutation of superoxide radicals to hydrogen peroxide and molecular oxygen [30]. Exposure to Aluminium also enhanced lipid peroxidation in plasma, testes and liver [22] and lowered plasma and testicular testosterone levels in mice [21]. Authors suggested that the severe reduction in male fertility following Aluminium administration might result from excessive Aluminium accumulation in the testes and low testosterone concentrations. Moreover, smilar studies found over productive of ROS, which can be detrimental to sperm and is associated with male infertility, and thus spermatoxic effect might be due to Aluminium induced free radicals [23].

There is evidence implicating androgenic hormones involved in mechanisms of aluminium toxicity on male reproduction. Studies also reported that Aluminium administration significantly increased nitric oxide (NO) production and decreased both testicular adenosine 3′, 5′-cyclic monophosphate (cAMP) and testosterone levels. Excessive NO, activated inducible NO synthase (NOS) which may be involved in reproductive toxicity of aluminum, hence reducing rate and motility of sperm cells, increasing their morphological abnormalities, and suppressing testosterone secretion in male rats**[**21]. Likewise, these effects of Aluminium may be attributed to Aluminium ability to cross the blood-testis barrier, after inducing oxidative stress and lipid peroxidation that damages the biological membranes of the testes. This in turn causes the degeneration of the spermatogene, which disrupts spermatogenesis and reduces sperm counts [31]. Also, the increase in TBARS can bring negative effects on motility and sperm-oocyte fusion [32**]**. Furthermore, increased ROS subsequently attack almost all cell components including lipid membrane and produce lipid peroxidation [33].

Another mechanism for Al induced oxidative stress is lipid per oxidation. Malondialdehyde (MDA) is a well known lipid peroxidation indicator and found to be increased in testis and epididymis after Al exposure [24, 32]. Increase lipid peroxidation might be caused by interference with mineral metabolism/ distribution. The capacity of Aluminium to displace other biological cations such as calcium, iron, zinc, copper and magnesium from their binding sites is a potential target for the adverse effects of Aluminium [34]. Intraperitoneal injection of Al chloride in male mice for 2 weeks significantly increased the testicular Aluminium burden, broke the balance of essential minerals Zn, Cu and Fe which results to an increased lipid peroxidation, as well as decreased testis ACE (testis-specific angiotensin-converting enzyme) activity [35].

There are accumulating reports that suggest that Aluminum interferes with iron homeostasis and severely impedes cellular metabolism. Aluminum is also known to favor the generation of an oxidative environment because of its ability to create a labile iron pool and to interact with membrane lipids**.** A rapid increase in serum Aluminium and the decrease of serum Fe levels were noted in Aluminium-treated animals; serum Aluminium and serum Fe levels were inversely correlated, which indicated that Fe metabolism may be influenced by Aluminium intoxication [36]. Aluminium ions replace iron and magnesium ions resulting in the reduction of Fe 2+ to ferretin. Free ions released from biological complexes by Aluminium can catalyze hydrogen per oxide decomposition to hydroxyl radical. This high hydroxyl radical reactivity is able to initiate lipid peroxidation [37]. The above evidence show that although Aluminium is a non redox metal, it can cause oxidative stress through multiple mechanisms.

However, excessive production of ROS above normal levels results in lipid peroxidation and membrane damage leading to loss of motility [38], damage to the acrosomal membranes and DNA oxidation, which render the sperm cell unable to fertilize the oocyte [39]. It is evidenced that the toxic impact of Aluminium chloride over the antioxidant system is more in the epididymis than the testis [40]. Aluminium is also known to generate Reactive nitrogen species (RNS). Al-induced nitric oxide (NO) by products may be an inhibitory regulator of steroidogenesis and sperm functions. NO is a free radical generated from the oxidation of L-arginine to L-citrulline by 3 isoforms of reduced nicotinamide adenine dinucleotide phosphate (NADPH)-dependent NO synthases (NOS). Excessive NOS may induce the production of large amounts of NO metabolites, hence reducing the rate and the motility of sperm cells and increasing their morphological abnormalities. NO may react with superoxide or hydrogen peroxide, resulting in the formation of peroxinitrite, hydroxyl radical, NO2, or singlet oxygen, which cause oxidation of sperm membrane lipids and thiol proteins. NO also may inhibit cellular respiration by nitrosylation of heme in mitochondrial enzymes, aconitase, and glyceraldehyde phosphate dehydrogenase, leading to a depletion of adenosine triphosphate and a consequent loss of motility by spermatozoa [41]. Several studies have shown that Al may induce changes in the activity of a number of biological antioxidants such as superoxide dismutase, catalase, and glutathione peroxidase/reductase system which have a considerable role in protecting the testis and sperm against peroxidative damage [42]. Sperm quality may deteriorate due to the alteration in antioxidant system both in vivo and in vitro by aluminium [20, 43].This clearly shows that the adverse effect of Al is not only affecting the testis impairing spermatogenesis, but it may also have severe impacts on sperm maturation and capacitation. It may also be assumed that though the spermatogenesis may be normal, the maturational events may be affected if the observed influence of Al is more in epididymis. However, it needs further studies at the level of sperm morphology and physiology.

Aluminium and blood testis barrier

The blood-testis barrier (BTB) is one of the tightest blood-tissue barriers in the mammalian body. The integrity of the blood-testis barrier (BTB) is essential to create a unique microenvironment for meiosis and the development of post-meiotic germ cells to isolate these events from the systemic circulation, which would otherwise develop anti-sperm antibodies. The BTB divides the seminiferous epithelium into the basal and the apical (adluminal) compartments. Meiosis I and II, spermiogenesis, and spermiation all take place in a specialized microenvironment behind the BTB in the apical compartment, but spermatogonial renewal and differentiation and cell cycle progression up to the preleptotene spermatocyte stage take place outside of the BTB in the basal compartment of the epithelium. However, the BTB is not a static ultrastructure. Instead, it undergoes extensive restructuring during the seminiferous epithelial cycle of spermatogenesis at stage VIII to allow the transit of preleptotene spermatocytes at the BTB [44].

Various findings showed that the nitric oxide produced by Aluminium is responsible for allowing Aluminum to enter the tight junctions that form the inter-Sertoli (so called blood-testis) barrier and accumulate in the testis **[**47**].** After entering into the testis, it damage germ and Sertoli cells, damaging the seminiferous epithelium, with a decrease in its height, thus altering normal spermatogenesis and sperm production **[**32, 45]. Kutlubay *et al* observed that thinner germinal epithelium of the seminiferous tubules and almost absence of spermatids and sperm numbers in the lumen in Aluminium (5 mg/kg body weight intraperitoneally in 2 ml saline treated) administered group [46].

Al and Histological alternation

Investigations in human and experimental animals reported an association between Aluminium exposure and male reproductive toxicity. Histological study on testes of male albino rats intoxicated with Aluminium for 90 days alone showed more exaggerated features of focal areas of spermatogenesis, arrest at the spermatid level, in the form of degenerative changes in the germinal cells together with few fragmented sperms in the lumen and acquired a thick, irregular basement membrane damage of testicular tubules and spermatogenesis which showed histological changes in the seminiferous tubule of that testis [14, 54]. Similar results are also reported that the effects of Alumiunium nitrite on mice are found to have spermatocytes and spermatids which show necrosism [15].

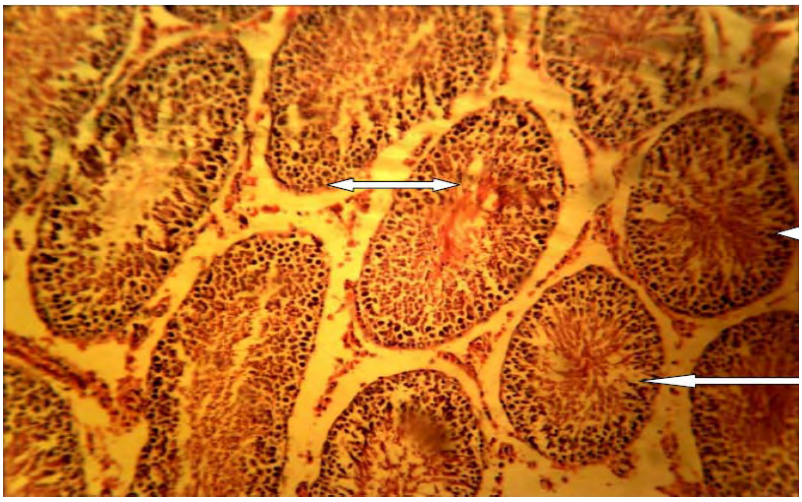
The majority of studies that utilized chronic doses of Aluminium reported significant reduction in weight gain, particularly in studies initiated in male animals. Decrease in water and food intake and transient diarrhea occurred, which resulted in the lowering of final body mass of animals in comparison to the controls (differences statistically significant) which are noted after three months of administration of Aluminium chloride to rats. The physiologic basis for this outcome is unclear, but it was reported that animals exposed to chronic doses of Aluminium consumed less food [16]. Whether general effects of Aluminium on metabolic processes depress metabolism or reduce nutritional efficiency remains to be resolved. In addition, studies also showed that a decrease in absolute and relative testes weights and seminal vesicles weights are found after Aluminum chloride ingestion [17, 58]. The decrease in the reproductive organs weights could be due to the decrease in testosterone level which was observed in the reports, may result from the oxidative damage induced in rat testes [18, 57].

Previous studies showed that, sexual behavior of male rats was suppressed after ingestion of aluminum chloride [17] and Necrosis of spermatocytes/ spermatids was also observed in the testes of mice exposed to Aluminium [19]. Poisoning by Aluminium chloride declines semen quality in vivo and vitro, and induced significant decrease in ejaculate volume, sperm concentration, total sperm output, sperm motility, total motile sperm per ejaculate, packed sperm volume, normal and live sperm, while the dead and the abnormal sperm were increased [20, 55,56]. Moreover, the observed decrease in sperm motility could be attributed partly to the concomitant reduction in testosterone production following Aluminium treatment [21, 22].

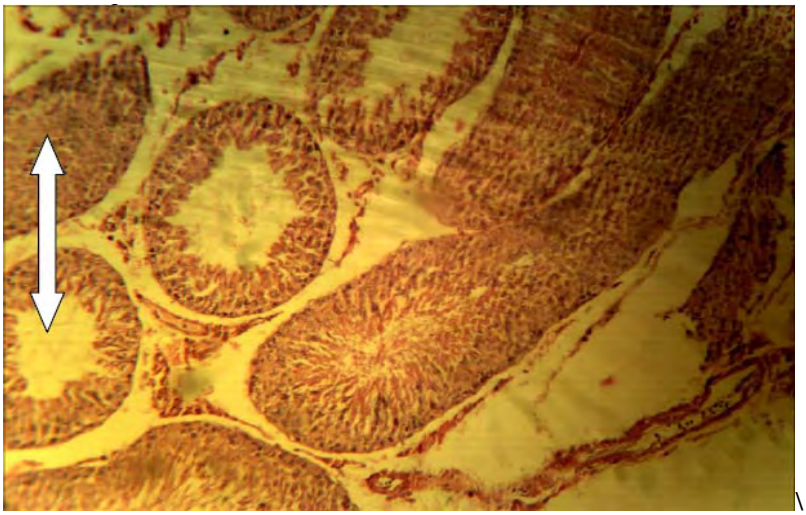
The testes are responsible for making testosterone, the primary male sex hormone, and for generating sperm. Within the testes are coiled masses of tubes called seminiferous tubules. These tubules are responsible for producing the sperm cells through a process called spermatogenesis [48, 49]. Histopathological examination of rats group orally administered Aluminium chloride showed apparent alteration in the testes, where it induced marked degeneration and necrosis of germ cells lining seminiferous tubules, as well as interstitial oedema and complete absence of germ cells [45**].** Also, findings revealed that deleterious effects and histopathological changes in testicular tissues after 2 weeks of Aluminium treatment, as well as noticeable spermatogenetic loss as necrosis in the spermatids and spermatozoa at the 5^{th} week of Aluminium treatment [50].

Similarly exposures of experimental animal to Aluminium, induce Coiling tail in rats' sperm, Cytoplasmic droplet in rats' sperm hyperemic blood vessel, interstitial edema, and Leydig cell proliferation [51]. In the study of Chinoy *et al*, treatment of mice with NaF and Aluminium for 30 days caused marked changes in the histology of both the caput and cauda epididymides [52]. Disruption of epithelium with pycnotic cell nuclei, clumping of stereocilia, reduction in sperm density, and cell debris in the lumen were the major alterations as compared to controls. It is likely that these structural alterations would affect its epithelium and biochemical makeup and subsequently its internal milieu thereby making it nonconducive for sperm maturation and survival. In the Al-treated group, the germinal epithelium of the seminiferous tubules was thinner in places and spermatids were almost absent; sperm numbers were low and there were no sperm in the lumen. In the Aluminium treated rats, histopathologic examinations revealed marked lesions in seminiferous tubules of testis [52].

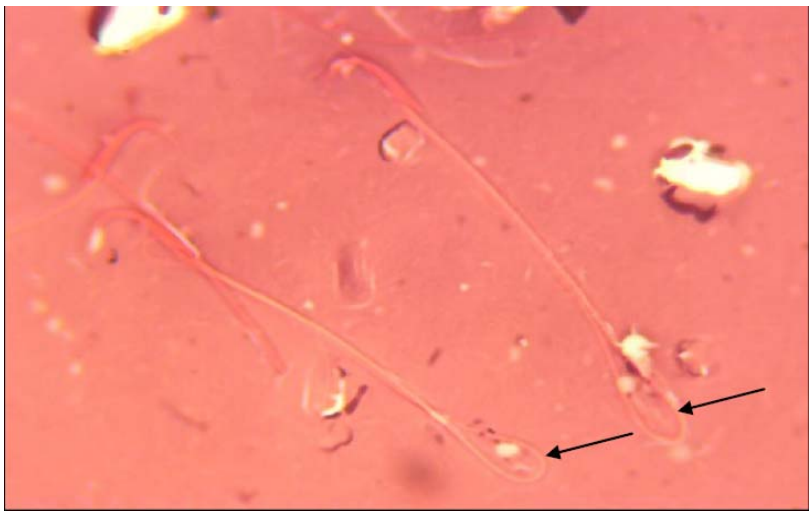
This damage effect also explained by Yousef and Salama who reported that oxidative stress results from the production of oxygen radicals in excess of the antioxidant capacity of the stressed tissue **[**24]. Many conditions or events associated with male infertility are inducers of oxidative stress, which leads to an increase in germ cell apoptosis and subsequent hypospermatogenesis, such as stress condition, which cause changes in the dynamics of testicular microvascular blood flow, endocrine signaling, and germ cell apoptosis. Moreover, reactive oxygen species and bimolecular oxidative damage, may contribute to male infertility by reducing sperm function [53]. Figure 2-3 shows some of the histological observations of aluminium induced male reproductive toxicity in various laboratory animals.



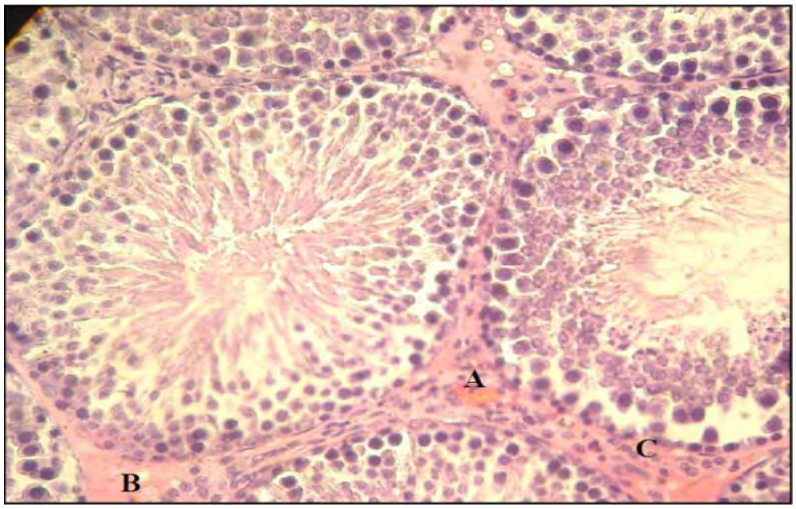
Figuer – 1; Photomicrograph of section in the normal testis of Control group I showing many seminiferous tubules (double arrow) with narrow lumina (arrows) and stratified epithelial lining .X100 H&E. (adapted from Buraimohet.al, *2012)*



Figuer – 2; Photomicrograph of section in the testis of group V showing distorted seminiferous tubules with loss of normal distribution of epithelial linning and vacuolar cytoplasm (double arrow). (adapted from Buraimohet.al, *2012)*



Figuer – 3; Coiling tail in rats sperm treated with AlCl3 (80mg/gm B.W.) for 30 days (eosin – nigrosin stain) 1300 x. (adapted from Entissar et al., 2009)



Figuer – 4; Histological section of testis from AlCl3 treated group (80 mg/kg B.W.) for 30 days showing hyperemic blood vessel (A), interstitial edema (B), Leydig cell proliferation (c). H.&E. (Mag. 370 x). adapted from Entissar et al., 2009)

Conclusion

The results of the present review provide evidence of adverse effects of Aluminium on certain reproductive parameters like sperm motility, viability and count, histology of testis and epididymis, as well as the reproductive hormone levels at various exposure levels. We further concluded on the basis of previous studies, that induction of oxidative stress, alteration in membrane functioning and cell signaling might be the possible mode of action by which Aluminium exert male reproductive disorders.

Abbreviations

GPX: Glutathione peroxides, MDA: Malondialdhyde, ROS:Reactive oxygen species, SOD: Superoxide dismutase, TBARS: Thiobarbituric acid reactive substances, NO: Nitric oxide; CAMP: Cyclic monophosphate, NOS: Nitric oxide synthase, ACE: Angiotensin converting enzyme, BTB: Brain test barrier

Competing interests

The author declare that they have no competing interests.

Authors' contributions

I proceeded with the literature review and drafted the paper and providing guidance, critical assessment and peer review of the writing. The author has given his final approval of this version to be published. The author read and approved the final manuscript.

Acknowledgements

The present review was supported by the Department of Anatomy and Histology, Institute of Bio-Medical Sciences, College of Health Sciences, Mekelle University - Mekelle, Ethiopia. I would like to thank my friend Dr. Cerilo N. Desmose for his friendly cooperate and giving me constructive ideas. I gratefully and foremost thank God who blessed my life and I pray for His will to provide me endless success.

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