International Journal of Advanced Biochemistry Research

ISSN Print: 2617-4693
ISSN Online: 2617-4707
NAAS Rating (2025): 5.29
IJABR 2025; 9(8): 175-179
www.biochemjournal.com
Received: 22-05-2025
Accepted: 25-06-2025

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Effect of excess fluoride exposure on growth rate and hemato-biochemical parameters in broiler chicks

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DOI: https://www.doi.org/10.33545/26174693.2025.v9.i8c.5127

Abstract
In the present study, 30 broiler chicks were randomly divided into two equal groups (Gr I and Gr II). Gr I chicks received drinking water (fluoride conc 0.9 ppm) and standard broiler starter (up to 3 weeks of age) and finisher ration (mean fluoride concentration 4.7 and 4.5 ppm, respectively) to serve as negative control, while Gr II received water containing 400 ppm fluoride and feed similar to Gr I. Body weight was measured and blood samples were collected on day 0, 20 and 40 of the experiment. On day 20, the mean body weight of Gr II chicks was 4.32% lower, while on day 40, it was 7.49% lower in comparison to Gr I. Hemoglobin concentrations in Gr II on day 20 and 40 were significantly (p<0.05) lower than corresponding values in Gr I. RBC count and PCV were also lower, but WBC counts were higher in Gr II in comparison to corresponding values in Gr I. Furthermore, significant increase in aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), creatinine and urea nitrogen were recorded in Gr II on day 40. Results suggested that excess fluoride (400 ppm or more) exposure in chick have suppressive effects on growth rate and erythropoiesis, increase in leukocyte count and level of enzymes related to liver and kidney functions.

Keywords: Blood-biochemistry, chick, fluoride, growth-rate, hematology, toxicity

Introduction
Small quantity of fluoride (F) is essential for bone and teeth mineralization, fertility maintenance, hematopoiesis and activation of specific enzymes such as adenyl cyclase, acid phosphatase, alkaline phosphatase, and isocitrate dehydrogenase (WHO 2000) [33]. However, prolonged ingestion of toxic doses of fluoride compounds by human, animals and birds can cause chronic F toxicity, commonly referred as fluorosis (Ranjan and Ranjan 2015) [21]. Human and animals in more than 20 countries across the globe are reported to suffer from fluorosis (WHO 2000) [33]. In India, high levels of F in drinking water have been reported to cause endemic fluorosis in human population in at least 17 states (Susheela, 1999) [28].
Susceptibility to fluorosis, varies among different animal species; cattle are the most susceptible followed by sheep, horses, pigs, rabbits, rats, guinea pigs and poultry (Shupe and Olson, 1971) [25]. Despite high tolerance to excess fluoride intake, adverse effects on growth and production potential in poultry following excess F exposure have been widely investigated in the past (Hauck *et al.*, 1933; Lundy *et al.*, 1992; Deng *et al.*, 2014 and Talpur *et al.*, 2022) [9, 14, 5, 29]. However, a state of confusion persists due to large variations in reported findings. In a study, it was found that 500 ppm fluoride in diet results into 8% reduction and 1000 ppm fluoride results into 21% retardation in growth rate in chicks, though both levels of F in diet do not alter liver and kidney enzyme activities (Wever *et al.*, 1969) [30]. But another study in chicks reported marked changes in enzymes related to liver and kidney functions in chicks exposed to feed containing 800 and 1200 ppm fluoride (Deng *et al.*, 2014) [5]. The present study, therefore aimed to study effects of excess fluoride intake through drinking water on growth rate, change in hematology and blood biochemistry in chicks.

Materials and Methods
The present research was carried out on 30 broiler chicks (Vencobb strain). Day old chicks were procured and housed in the Poultry Farm, College of Veterinary and Animal Sciences,

RAJUVAS, Bikaner in electric hover brooder in deep litter system and acclimatized for 5 days. Chicks were given standard broiler starter (up to 3 weeks of age) and finisher ration (with mean F concentration 4.7 and 4.5 ppm, respectively) and drinking water *ad libitum*. On day 6 (Day of observation 0), chicks were randomly divided into two equal groups. Group I received normal dirking water (F conc. 0.9 ppm) to serve as negative control, while group II received fluoridated drinking water (400 ppm F conc.) *ad libitum* for 40 days. Body weights were measured and blood samples were collected on day 0, 20 and 40 from wing vein for estimation of hemato-biochemical parameters and estimation of calcium, phosphorus, magnesium and fluoride concentrations. For day 0, pooled blood samples from 3 chicks were collected. The experimental protocol was approved by The Institutional Animal Ethics Committee of College of Veterinary and Animal Sciences, RAJUVAS, Bikaner. Different hematological parameters including haemoglobin (HB), total leukocyte count (TLC), total erythrocyte count (TEC) and packed cell volume (PCV) were estimated as per standard procedures (Jain, 1986). Activity of Alkaline phosphatase (ALP), Aspartate transaminase (AST), Alanine transaminase (ALT) were estimated in serum using diagnostic kits supplied by Span Diagnostic Ltd., India.

Plasma fluoride concentration was measured by the method of Cernik *et al.* (1970) using digital ion-analyzer equipped with a fluoride specific electrode (Orion Star A 214 Benchtop PH/ISE Meter, Thermo Scientific, USA). The electrode was filled with electrode filling solution and the quality control criterion was met using repeated slope determination (W.H.O., 1984). The instrument was calibrated using 0.01 µg/ ml, 0.1 µg/ ml and 1 µg/ ml fluoride standard solutions. Plasma samples were diluted with TISAB II, mixed thoroughly, and F concentration was estimated (Ranjan *et al.*, 2021) [22]. Likewise, fluoride concentration in water sample was estimated after mixing with TISAB II (Ranjan and Ranjan 2015) [21]. The data obtained was analyzed statistically as per the standard methods using SPSS, version 10.0, statistical software (SPSS 1997) [26].

Results and Discussion

In the present study, sodium fluoride was used as a source for excess fluoride intake. The relative aqueous solubility of fluoride compound has great impact on absorption of fluoride from gastro-intestinal tract (WHO 2002) [31]. Sodium fluoride has high water solubility, hence results into rapid increase in blood and urine fluoride concentration in rabbits (She *et al.*, 2002 and Reddy *et al.*, 2003) [24, 23] and birds (Miao *et al.*, 2019) [16]. Therefore, this is the most commonly used fluoride compound used for induction of experimental fluorosis (Ranjan and Ranjan 2015) [21]. Both feed and drinking water are equally effective as a medium for excess fluoride exposure as changes in feed and water consumption and growth rate in chicks were found similar following exposure of excess fluoride in equivalent doses either through drinking water or through feed (Raica *et al.*, 1957) [19].

Feed and water intake in both groups of chicks were almost normal during the entire experiment period. In corroboration with the present findings, Hauck *et al.* (1933) [9] reported that no depression in appetite was recorded in chicks given 0.15 per cent sodium fluoride in feed. However, higher doses may affect as Weber *et al.* (1969) [30] found that feed intake in chicks reduces when they are exposed to 500 ppm or more fluoride in feed, either due to lowered energy needs or due to impairment in the appetite centers in the brain.

Changes in plasma fluoride concentration in negative control and fluoride intoxicated chicks are depicted in Fig 1. On day 0, the values were statistically comparable, while on day 20, it was 48.02 per cent higher in Group II as compared to negative control (Gr I). On day 40, plasma fluoride concentration in Gr II was approximately nine times the value recorded in Gr I. The plasma fluoride level in Gr II on both the observation days differed significantly (p<0.05) from corresponding levels in Gr I. Fluoride concentration in plasma is a good indicator of blood F content as nearly 75% of F remains free in plasma (Deng *et al.*, 2014) [5]. It reflects current intake of fluoride from feed and water. Significant increase in plasma fluoride concentration on day 20 and 40 following excess fluoride exposure in birds suggested high bioavailability of fluoride in the present study. The peak of fluoride concentration in plasma is reached quickly as a result of a rapid pH dependent absorption in the stomach (Azab *et al.*, 2018) [3]. The plasma fluoride levels declines mainly due to renal excretion and F uptake by hard tissues (Ranjan and Ranjan 2015) [21].

Changes in body weight of experimental chicks are depicted in Fig 2. On day 20, the mean body weight of fluoride intoxicated chicks was 4.32% lower in comparison to control chicks, while on day 40, it was 7.49% lower. Both these changes were statistically significant (p<0.05). Several studies conducted in the past reported marked inhibition in growth rate of baby chicks following exposure to excess fluoride. A reduction of 8% in growth rate was recorded in chicks given 500 ppm fluoride, while 21% reduction in growth rate was noted in chicks given 1000 ppm fluoride in feed for four weeks. In another study, 0.3 per cent sodium fluoride addition in starter ration resulted into significant reduction in growth rate of young chicks, though the effect was less prominent in older chicks (Hauck *et al.*, 1933) [9]. Weber *et al.* (1969) [30] reported that feed intake in chicks reduces when they are exposed to 500 ppm or more fluoride in feed, either due to lowered energy needs or due to impairment in the appetite centers in the brain. Luo *et al.* (2012) [15] found that the diet containing fluoride between 22.2 mg/kg to 200 mg/kg causes slight reduction in body weight as compared to the healthy birds due to negative effect on mucosal immune function of the intestine. Aydogen *et al.* (2018) [2] also found a significant decrease in body weight of broilers, fed a diet containing 800 mg/kg of Fluoride, when compared to the control group (normal diet).

Fluoride is a well-known inhibitor of numerous enzymes, and is reported to affect protein synthesis by destruction of polypeptide chains and weakness of amino-acid bindings in protein (Helgeland 1976 and Deng *et al.*, 2014) [10, 5]. Excess fluorine also interferes with Mg, Mn, Fe, Mo, Cu and Zn metabolism, vitamin B12 synthesis and folic acid activity (WHO 2000) [33]. Protein utilization decreases with increasing dietary fluoride (Olkowski 2009 and Ranjan and Ranjan 2015) [18, 21]. Impairment in mineral and vitamin utilization as well as impaired protein synthesis and utilization might have contributed towards lower weight gain in birds exposed to excess fluoride in the present study. Another possible reason may be impairment in duodenal and proventriculus functions, as histopathological changes were recorded in these organs in chicks exposed to excess fluoride by several workers (Hauck *et al.*, 1933; Aydogan *et al.*, 2018 and Talpur *et al.*, 2022) [9, 2, 29]

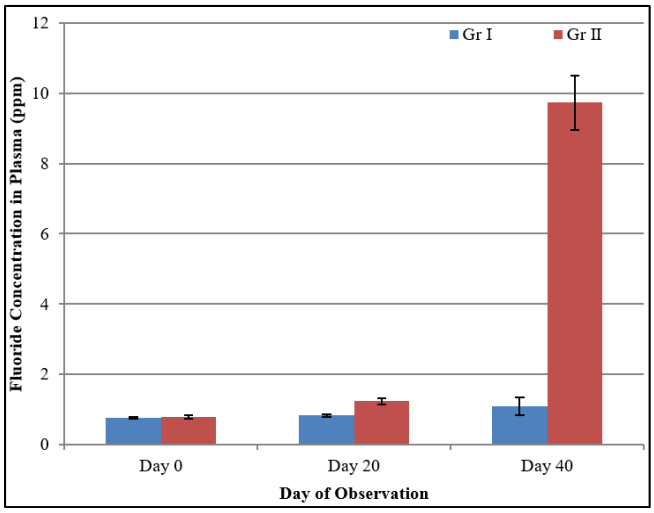

Fig 1: Changes in plasma fluoride concentration (ppm) in chicks

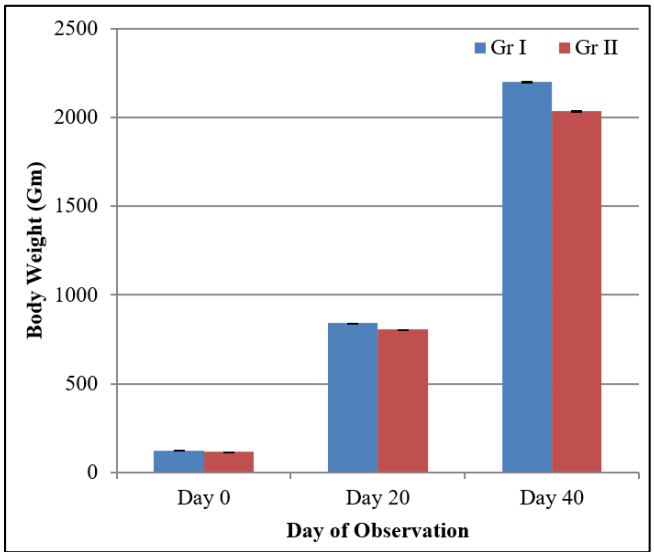

Fig 2: Changes in body (gm) weight of chicks

Mean (±S.E.) values of different hematological parameters in chick are given in Table 1. Hemoglobin concentration on day 20 as well as day 40 were significantly (p<0.05) lower in Gr. II animals in comparison to corresponding values in Gr I. Also, the RBC count and PCV were lower in Gr II in comparison to Gr I on day 20 as well as day 40. However, the WBC counts were higher in Gr II than Gr I on day 20 as well as day 40. These changes suggested that excess fluoride exposure in chicks resulted into suppressive effects on erythropoiesis along with increased leukocyte count. We could not find any study investigating hematological changes in fluorosis in chicks to compare results of the present study. Perhaps these changes were induced due to oxidative stress that supervenes in fluorosis (Giri *et al.*, 2016) [7].

Mean (±S.E.) values of different biochemical parameters in different treatment groups of chicks are given in Table 2. Significant (p<0.05) increase in ALT, AST and ALP activities in fluoride intoxicated chicks (Group I) suggested excess fluoride induces hepatocellular injuries. Marked increase in AST, ALT and ALP activities were also recorded in chicks who received feed containing 800 and 1200 mg F/ kg for a period of 42 days (Deng *et al.*, 2014) [5]. Since liver is an active site of metabolism, it is highly vulnerable for various toxicities including those induced by excess F intake (Bouaziz *et al.*, 2006) [4]. However, the response varies with dose and duration of F exposure, and even with animal species (Deng *et al.*, 2014) [5]. ALP is also the marker enzyme for bone pathology. Increased ALP activities in F intoxicated chicks indicated toxic effects of excess F on osteoblasts and osteocytes. Similar pattern of increase in ALP level in blood was recorded in chicks receiving excess dietary F for 42 days (Deng *et al.*, 2014) [5]. In the present study, significant increase in creatinine and urea nitrogen was recorded in fluoride intoxicated chicks. Creatinine concentration in serum or plasma acts as a biomarker for kidney function in human, domestic animals and birds (Duncan *et al.*, 2001 and Deng *et al.*, 2014) [6, 5]. Increase in creatinine and urea in fluoride toxicity has also been reported in mice (Al-Harbi *et al.*, 2014) [1], rats (Giri *et al.*, 2015) [21], rabbits (Ranjan *et al.*, 2009) [21], pigs (Zhan *et al.*, 2016) [34] and poultry (Deng *et al.*, 2014) [5]. In line to the present findings, increase in plasma creatinine levels were also recorded in poultry fed with 800 mg F/ kg or more in feed (Deng *et al.*, 2014) [5]. Recently, a study reported marked shrinkage of glomeruli with widened bowman's space along with inflammatory cellular infiltration in kidney of broiler chicks following exposure to 200 mg sodium fluoride/ liter drinking water for 18 days (Talpur *et al.*, 2022) [29]. Urine is the major route of F removal from the body, hence kidney plays an important role in protection against the toxic effects of excess F intake (Inkielewicz and Krechniak 2003 and Deng *et al.*, 2014) [5]. In healthy individuals, about 50% of ingested fluoride is excreted by kidneys. The renal system, therefore, appears to be at high risk of fluoride toxicity than most other soft tissues (N.R.C., 2006). Fluoride inhibits various enzyme systems in kidneys (Jankaurkar, 1974) [13] and decreases Na, K and ATPase activities (Suketa and Terui, 1980) [27] thereby inducing toxic effects.

Table 1: Changes in hematological parameters in chicks on different observation period

Parameter	Group	Day 0	Day 20	Day 40
Hb (gm/dl)	I	9.93 ± 0.24^{aA}	11.7 ± 0.289^{bB}	11.9 ± 0.058^{bB}
	II	9.75 ± 0.65^{aA}	10.6 ± 0.173^{aB}	9.4 ± 0.115^{aA}
RBC ($\times10^6/\mu L$)	I	2.117 ± 0.064^{aA}	2.39 ± 0.012^{bB}	2.41 ± 0.006^{bB}
	II	2.108 ± 0.091^{aA}	2.241 ± 0.046^{aB}	1.933 ± 0.017^{aA}
WBC ($\times10^3/\mu L$)	I	19.75 ± 2.335^{aA}	20.53 ± 4.163^{aA}	22.97 ± 0.055^{aA}
	II	20.05 ± 2.645^{aA}	21.71 ± 1.466^{bA}	25.65 ± 2.335^{bB}
PCV (%)	I	23.016 ± 9.742^{aA}	24.64 ± 0.004^{bA}	24.31 ± 0^{bA}
	II	24.05 ± 9.432^{aB}	23.12 ± 0.005^{aB}	21.54 ± 0.00^{aA}
Values bearing different superscript in small letters in a column and capital letters in a row differ significantly ($P \leq 0.05$)				

Table 2: Changes in ALP, AST, ALT, creatinine and urea nitrogen in plasma of chicks (in different treatment groups and control

Parameter	Group	Day 0	Day 20	Day 40
ALP (U/L)	I.	705.33 ± 10.47^{aA}	773.3 ± 8.71^{aA}	963.33 ± 73.62^{aB}
	II.	702.33 ± 11.54^{aA}	990.66 ± 41.70^{bB}	1264.33 ± 90.81^{bC}
AST (U/L)	I.	146.08 ± 0.639^{aA}	147.227 ± 0.716^{aA}	151.642 ± 1.432^{aB}
	II.	147.08 ± 0.611^{aA}	167.027 ± 0.91^{bB}	177.672 ± 1.21^{bC}
ALT (U/L)	I.	12.497 ± 0.015^{aA}	13.27 ± 0.072^{aA}	15.885 ± 0.042^{aB}
	II.	12.654 ± 0.015^{aA}	16.577 ± 0.217^{bB}	23.727 ± 0.699^{bC}
Creatinine (mg/dl)	I.	0.427 ± 0.012^{aA}	0.513 ± 0.023^{aA}	0.612 ± 0.022^{aA}
	II.	0.423 ± 0.067^{aA}	0.553 ± 0.041^{bA}	0.772 ± 0.061^{bB}
Urea nitrogen (mg/dl)	I.	0.340 ± 0.055^{aA}	0.423 ± 0.105^{aB}	0.437 ± 0.162^{aB}
	II.	0.346 ± 0.067^{aA}	0.457 ± 0.301^{aB}	0.603 ± 0.571^{bC}
Values bearing different superscript in small letters in a column and capital letters in a row differ significantly ($P \leq 0.05$)				

On the basis of results of the present study, it can be concluded that excess fluoride exposure (400 ppm or more) through drinking water in chicks can reduce the growth rate, and induce changes in hematological profile and increased blood levels of enzymes related to liver and kidney functions.

References

1. Al-Harbi MS, Hamza RZ, Dwari AA. Sodium fluoride induced antioxidant defense impairment and impaired renal biomarkers and the ameliorative role of selenium and curcumin in male mice. Asian Pac J Trop Dis. 2014;4(Suppl 2):S990-S997. https://doi.org/10.1016/S2222-1808(14)60771-4
2. Aydogan I, Yildirim E, Kabakci R, Sumer T. The effect of fluoride toxication on duodenum, jejunum and ileum of broilers. J Poult Res. 2018;15:34-39.
3. Azab AE, Albasha MO, Jbireal JM, Adwas AA. Sodium fluoride induces hepato-renal oxidative stress and pathophysiological changes in experimental animals. Open J Apoptosis. 2018;7:1-23.
4. Bouaziz H, Ketata S, Jammoussi K, Boudawara T, Ayedi F, Ellouze F, *et al.* Effects of sodium fluoride on hepatic toxicity in adult mice and their suckling pups. Pestic Biochem Physiol. 2006;86:124-130. http://dx.doi.org/10.1016/j.pestbp.2006.02.004
5. Deng Y, Cui H, Peng X, Fang J, Zuo Z, Deng J, *et al.* Effect of high dietary fluoride on serum biochemistry and oxidative stress parameters in broiler chickens. Health. 2014;6:1840-1848.
6. Duncan L, Heathcote J, Djurdjev O, Levin A. Screening for renal disease using serum creatinine: Who are we missing? Nephrol Dial Transplant. 2001;16:1042-1046. http://dx.doi.org/10.1093/ndt/16.5.1042
7. Giri A, Bharti VK, Angmo K, Kalia S, Kumar B. Fluoride induced oxidative stress, immune system and apoptosis in animals: A review. Int J Bioassays. 2016;5(12). doi:10.21746/ijbio.2016.12.0011
8. Giri DK, Ghosh RC, Kashyap DK, Dewangan G, Maiti SK. Haemato-biochemical alterations in subacute oral toxicity of sodium fluoride in Wistar rats. J Anim Res. 2015;5:595-598. https://doi.org/10.5958/2277-940X.2015.00100.X
9. Hauck HM, Steenbock H, Lowe JT, Halpin JG. Effect of fluorine on growth, calcification and parathyroids in the chicken. Poult Sci. 1933;12:242-249.
10. Helgeland K. Effect of fluoride on protein and collagen biosynthesis in rabbit dental pulp *in vitro*. Scand J Dent Res. 1976;84:276-285.
11. Inkielewicz I, Krechniak J. Fluoride content in soft tissues and urine of rats exposed to sodium fluoride in drinking water. Fluoride. 2003;36:263-266.
12. Jain NC. Schalm's Veterinary Hematology. 4th ed. Lea & Febiger; 1986.
13. Jankaurkar J. Effects of fluoride on the kidney (a review). Fluoride. 1974;7:93-105.
14. Lundy MW, Russell JE, Avery J, Wergedal JE, Baylink DJ. Effect of sodium fluoride on bone density in chickens. Calcif Tissue Int. 1992;50:420-426.
15. Luo R, Liu RG, Ye C, Yu YN, Guan ZZ. Total knee arthroplasty for the treatment of knee osteoarthritis caused by endemic skeletal fluorosis. Chin J Tissue Eng Res. 2012;16(9):1555.
16. Miao LP, Li LL, Zhu MK, Dong XY, Elwan HAM, Zou XT. Excess dietary fluoride affects laying performance, egg quality, tissue retention, serum biochemical indices, and reproductive hormones of laying hens. Poult Sci. 2019;98:6873-6879.
17. National Research Council (NRC). Fluoride in Drinking Water: A Scientific Review of EPA's Standards. Washington, DC: National Academies Press; 2006. p. 236.
18. Olkowski AA. Livestock Water Quality: A Field Guide for Cattle, Horses, Poultry and Swine. University of Saskatchewan; 2009. ISBN: 978-1-100-12443-8.
19. Raica N, Heywang BW, Vavich MG, Kemmerer AR. The effect of fluoridated water on chick growth. Poult Sci. 1957;36:1027-1030.
20. Ranjan R, Swarup D, Patra RC, Chandra V. *Tamarindus indica* L. and Moringa oleifera M. extract administration ameliorates fluoride toxicity in rabbits. Indian J Exp Biol. 2009;47:900-905.
21. Ranjan R, Ranjan A. Fluoride Toxicity in Animals. Springer International Publishing; 2015. ISBN: 978-3-319-17511-9.
22. Ranjan A, Nabi J, Ranjan R. Normal serum fluoride concentration in dromedary camel (*Camelus dromedarius*). Biol Trace Elem Res. 2021;199(11):4129-4132. doi:10.1007/s12011-020-02534-9
23. Reddy GB, Khandare AL, Reddy PY, Rao GS, Balakrishna N, Srivalli I. Antioxidant defense system and lipid peroxidation in patients with skeletal fluorosis and in fluoride intoxicated rabbits. Toxicol Sci. 2003;72:363-368.
24. She YX, Gesang DZ, Tian FY, Suo LZ. Analysis of fluorine concentration in rabbit blood and trace elements in its muscles. Chin J Anim Quarantine. 2002;19:23-24.

25. Shupe JL, Olson AE. Clinical aspects of fluorosis in horses. J Am Vet Med Assoc. 1971;158:167-174.
26. SPSS Inc. SPSS for Windows, Version 10.0. Chicago, IL: SPSS Inc.; 1997.
27. Suketa Y, Terui Y. Adrenal function and changes in renal (Na and K)-ATPase activities of fluoride intoxicated rats. Fluoride. 1980;13:148-150.
28. Susheela AK. Fluorosis management program in India. Curr Sci. 1999;77(10):1250-1256.
29. Talpur BR, Nizamani ZA, Leghari IH, Tariq M, Rehman A, Kumbhar S. Hepato-nephrotoxic effects of induced fluorosis in rabbits and broilers. J Anim Health Prod. 2022;10:214-220.
30. Weber CW, Doberenz AR, Reid BL. Fluoride toxicity in the chick. Poult Sci. 1969;48:230-235.
31. World Health Organization (WHO). Fluorides. Environmental Health Criteria 227. Geneva: WHO; 2002.
32. World Health Organization (WHO). Fluorine and Fluorides. Environmental Health Criteria, Series 36. Geneva: WHO; 1984.
33. World Health Organization (WHO). Fluoride in Drinking Water. Geneva: WHO; 2000.
34. Zhan XA, Wang M, Xu ZR, Li JX. Toxic effects of fluoride on kidney function and histological structure in young pigs. Fluoride. 2016;39(1):22-26.