Egyptian Journal of Rabbit Science, 28 (1): 63-92(2018)

PHYSIOLOGICAL, REPRODUCTIVE AND PRODUCTIVE PERFORMANCE OF RABBIT DOESAS INFLUENCED BY N-ACETYLCYSTEINE ADMINISTRATION

G. Ashour [1*]; Samah M. Abdel-Rahman [2]; W. A. Morsy [2]; Noha M. Abdel-Azeem [2] and Safaa A. Barakat [2]

1- *Animal ProductionDepartment, Faculty of Agriculture, Cairo University, Giza, Egypt*

2- *Animal Production Research Institute, Agricultural Research Center, Giza, Egypt *Corresponding author: gashour57@yahoo.com*

The present study was carried out in Rabbit Research Unit at Sakha Research Station located in Kafr El-Shiekh governorate, Egypt to assess the impact of N-acetylecysteine (NAC) administration on the physiological, reproductive and productive performance of rabbit does. A total number of 21 pregnant, healthy, primiparous New Zealand White (NZW) rabbit does aged between 5-6 months with an average initial body weight (BW) of 3052 g were used. They were divided into three equal groups. The first group (G1) was served as control group without any administration. The second and third groups (G2 and G3) were injected subcutaneously with 50 and 100 mg NAC / kg BW, respectively. The injection with NAC doses started on day 14 of pregnancy and continued for seven consecutive days. The experiment lasted continuously for three months.

The obtained results showed that, *NAC treatment reduced the oxidative stress in pregnant rabbit does, G2 and G3 had the highest values of GST and the lowest values of both MDA and H_2O_2 in comparison with those of G1.Total protein, albumin, globulin and A/G ratio did not significantly affected by NAC injection and tended to increase with pregnancy progress. In contrast, level of triglycerides decreased ($P<0.05$) in G2 and G3 than that of G1 and declined with progress of gestation till kindling. Treated groups decreased their blood urea nitrogen (BUN) values and increased their creatinine (CR) levels than those of G1. With progress of pregnancy, levels of BUN tended to decrease and CR levels tented to increase. Both transaminase enzymes (AST and ALT) activities decreased by NAC treatment and by pregnancy progress, particularly in G3.*

The changes in live BW of does in the three groups across the experimental period were insignificant. NAC injection achieved

improvement in suckling kits' weight during all the experimental days. At weaning day, G2 and G3 had heavier kits' weight than those in G1 by 26 and 20 %, respectively. Litter size increased obviously due to NAC treatment by 19 to 35 % in G2 and by 5.5 to 23.1 % in G3 than that in G1 during the all experimental days. Mortality rate reduced by NAC injection being the lowest in G2 (4.7 %) followed by G3 (11.2%) and the highest in G1 (23.6 %). Total milk yield was increased significantly in G3 and insignificantly in G2 compared to that of G1 by 17.5 and 4.5 %,respectively. The high dose was more effective in promoting milk production. The effect of NAC treatment on all milk components was insignificant, except milk lactose. From the first wk to the last wk, milk composition (%) of milk protein, milk lactose, milk total solids and milk solids not fats increased (P<0.05) whereas milk fat decreased.

In conclusion, this study proved not only the effectiveness, but also the safety of NAC application and its capability to improve rabbit's performance particularly with high dose (100 mg/kg BW). Further studies are urgently needed to confirm our findings.

Key words: N-acetylcysteine, antioxidant status, metabolites, kidney and liver functions, litter size & weight, mortality rate, milk yield & compositions.

In recent years rabbits industry in Egypt has a great interest as one of the small livestock commercial projects that can play an important role (after poultry industry) in solving meat shortage (Mohammed *et al*., 2013). The rabbits have the ability to utilize up to 30% of crude fiber and convert 20% of the intake protein into meat, which considered as a vital source of protein and its content of fat is low (Hassan *et al*., 2017). Meanwhile, rabbit farming in Egypt is still unstable because they facing a serious problems (diseases, heat stress during summer season and poor feed quality). Therefore, they need a great attention to protect the industry from economic losses (Diab *et al*., 2003 and Mohammed *et al*., 2013).Many efforts have been done by the Egyptian scientists to improve and manage the rabbit industry. They used different antioxidant as feed additives through supplementation or administration, one of these antioxidants is N-acetyl cysteine (NAC). However, few reasechers used NAC and they were focusing on its therapeutic role in enhancing health and treating aflatoxins in rabbits as reported by Atef *et al*. (2016).

The NAC can be defined as, an intracellular glutathione(GSH) precursor that is currently one of the most studied antioxidants as it is endogenously synthesized basically in all cells. Furthermore, it has the ability in regulation of cell proliferation, regulation of immune responses, as well as regulation of leukotriene and prostaglandin metabolism precursor (Agostinis *et al*., 2014).In addition, NAC is a commercial product has been tested in human by many studies and reported its positive role in many diseases (Cam *et al*., 2008; de Andrade *et al*., 2015 and Gao *et al*., 2017). Furthermore, NAC was using in animal experiments and reported positive results, and was introduced orally(well accepted), intravenous or by inhalation (Gao *et al*., 2017).

In rabbits, Omar *et al*. (2012) reported the ability of NAC in reducing glucose level in induced diabetic rabbits by conferring protection to pancreatic ß-cells from reactive oxygen species (ROS) which causingß-cells toxicity and reduction in glutathione (GSH) production.Likewise, Atef *et al*. (2016) proved the ability of NAC in providing hepatic cell protection from cancer caused by aflatoxin B1 in induced aflatoxicosis in rabbit by using 50 µg of AF dissolved in 0.5 ml of olive oil/ animal daily for four weeks, then treated them with two different doses of NAC (250 and 500 mg/kg BW). They recommended that, treatment with a high dose of NAC may interfere with hepatic normal metabolic functions by reducing the elevated activity of ALT, AST and ALP (which considered a marker that expresses the severity of liver injury) and impairs liver recovery from aflatoxin B1hepatotoxicity. Also, they proved that NAC is considered today a critical demand to safe animal health.

Therefore, the impact of the performance enhancing effect of NAC on rabbits is very rare particularly under Egyptian conditions. Therefore, the present study was undertaken to evaluate whether NAC has beneficial role in enhancing the physiological, reproductive and productive performance in NZW rabbits under Egyptian conditions, especially since we did not find researches have been conducted in this area.

MATERIALS AND METHODS

The present study was carried out in Rabbit Research Unit at Sakha Research Station located in Kafr El-Shiekh governorate, Egypt, belongs to Animal Production Research Institute (APRI), Agricultural Research Center (ARC). The fieldwork was executed during the comfortable months of rabbit

production in Egypt from October to December. Meanwhile, the laboratory work was carried out in APRI labs.

1- Experimental animals and management:

In this experiment, a total number of 21 pregnant, healthy, primiparous New Zealand White (NZW) rabbit does aged between 5-6 months were used. The animals were housed individually in galvanized wire batteries in well ventilated indoor pens. Does were fed *ad libitum* at 8:00 and 15:00 for three weeks of physiological adjustment period. The rations satisfied the nutrient requirement of the does according to NRC (1977), provided 18% crude protein, 13.4% crude fiber and digestible energy 2500 kcal/ kg diet. Fresh and clean water was available *ad-libitum*. The pregnant does were randomly divided into three equal groups (7 does in each group). The first group (G1) was served as control group without any administration; their average body weight (BW) was 3078 ±70.2 g. The second and the third groups (G2 and G3) were injected subcutaneously with 50 and 100 mg N-acetyl cysteine (NAC) / kg BW, respectively. Their average BW was 3013 ±70.2 g and 3067±70.2 g, respectively. The NAC was purchased from commercial pharmacy and the injection with NAC doses waslasted for seven consecutive days according to Omer *et al*. (2012) and started on day 14 of pregnancy according to Schaefer *et al*. (2007). The experiment was lasted for three months continuously, started on October and ended on Novemberuntil the weaning age of the progeny.

2- Plasma biochemical analyses:

Blood samples (about 3 ml) were collected before one day of NAC injection (day 13 of pregnancy, placentation period according to Wahab *et al*. (2016),then on days 21, 28 of pregnancy (days of fetal growth, Wahab *et al*. (2016) and day of parturition. The samples were collected in heparinized tubes from each doe and were centrifuged at 3000 r.p.m. to get blood plasma that stored under -20°C until biochemical analysis. A colorimetric method was used to determine Glutathione-S-Transferase (GST), Malondialdehyde (MDA) and Hydrogen peroxide (H_2O_2) by using kits obtained from Bio-Diagnostic Company, Dokki, Giza, Egypt. Quantitative colorimetric determination of total protein (TP, g/dl), albumin (Alb,g/dl) and triglycerides (TG mg/dl) were executed by using kits of Stanbio Laboratory Inc, procedure No. 0280. (San Antonio, Texas, USA). Globulin concentration (Glb, g/dl) was calculated by subtracting Alb values from TP values. Albumin/ Globulin ratio (A/G ratio) was calculated. Kits from EGY- CHEM for lab technology (Badr City, Industrial

Area Piece 170 - Egypt) were used in determination of concentrations (mg/dl) of blood urea nitrogen(BUN) and creatinine (CR) as indicators for kidney functions. Activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) as indicators for liver functionswere determined colorimetricly using kits supplied by Sentinel Ch. SpA- Via Robert Koch, 2-20125 Milan- Italy. All determinations were performed according to the procedures outlined by the respective manufactures.

3- Body weight and litter size:

Pregnant does were reared to full gestation and to 30-day post-partum to determine the changes in their live BW. During pregnancy period, rabbit does were weighed using sensitive balance at day 14 from pregnancy, at day 28, at partum day and at weaning day. In addition, the litter size and weights were recorded from their birth and lasted concurrently with collecting milk samples. Mortality rate (MR) was estimated during the period from birth to weaning age.

4- Milk samples and analyses:

Milk yield (MY, g/d) was determined by calculating the difference in kit´s body weight before and after suckling. The amount of daily milk yield / doe (DMY, g/d)and the average of total milk yield (TMY) during the whole lactation period (four weeks) were determined. Milk samples were collected at weekly intervals and kept frozen at (-20◦ C) until the chemical analyses were executed. Percentages of milk fat (MF), lactose (ML), protein (MP), total solids (MTS) and solids not fat (MSNF) were determined by Milkoscan® analyzer (130 B, N. Foss Electronic, Denmark) at International Livestock Management Training Center at Sakha, Kafr El-Sheikh governorate.

5- Statistical analysis:

The collected data were subjected to two way analysis of variance to detect the effects of treatment(T) and time of collecting blood samples (sample date, SD) and their interaction (T*SD) using the general linear model (GLM) procedure of SAS **(SAS, 1999).**

The statistical model used was as follows:

$$Y_{ijk}= \mu + T_i + SD_j+(T*SD)_{ij} + e_{ijk}$$

Where: Y_{ijk}= the individual observation, μ = The overall mean, T_i= The effect of the treatments (i= 1,2,3), SD_j= the effect of time (j=1, 2, 3, 4), $(T*SD)_{ij}$= Effect of interaction between i^{th} treatments and j^{th} the days of gestation (ij =1,……..12), e_{ijk}= Random error associated with the individual.

The collected data of dam weights, litter size and weight were subjected to one-way analysis of variance to detect the effect of treatment with NAC.

The statistical model used was as follows:

$$Y_{ij} = \mu + T_i + e_{ij}$$

The differences among treatments, time and interaction means were separated according Duncan's Multiple Range Test (Duncan, 1955). The significance level was set at 5%.

RESULTS AND DISCUSSION

1. Physiological parameters:

1.1. Antioxidant status:

Treatment with NAC by two doses 50 (G2) and 100 (G3) mg / kg BW increased ($P<0.05$) the activity of GST than those of control group by 38.6 and 56.1 %, respectively. This increase could be attributed to the ability of NAC in increasing the activity of GST, which might be mediated by glutathione (GSH) synthesis (Kamboj *et al*., 2010). This incremental increase of GST activity caused a reduction in concentrations of $H_2O_2$by 13.3 and 35.6% in G2 and G3 compared to those in G1, respectively (Table, 1). The reason of H_2O_2 reduction may attribute to; GST is one of the most antioxidant enzymes, which play an active role in protecting cell from oxidative stress (OS) by detoxification of H_2O_2. Also, GST is catalyzing the conjugation of GSH with organic compounds such as hydroperoixdes. This explain the ability of GST in converting H_2O_2 to water (H_2O), thereby eliminate the hydroxyl radicals (OH^-) then the cell can scavenge the OS (Rao *et al*., 2013). In addition, a significant ($P<0.05$) reduction in concentrations of MDA (a key product of lipid peroxidation) by 23.8 and 33.3 % in G2 and G3 as compared to those in G1, respectively.

Therefore, the current study confirmed that NAC administration reduced the OS that occurring during gestation period. It is well established that, pregnancy is a critical period causing OS (Krieing and Loch-Caruso, 2001), because synthesis of prostaglandin which involved in embryo implantation leading to the presence of some free radicals (Hope *et al*., 1975). Furthermore, it could be noticed that the high dose of NAC treatment was more effective than that of low dose as observed in G3 (Table, 1). Activity of GST in does of G3 was insignificantly higher than that in does of G2 by 12.7%. On the other side, the decreases in levels of MDA and H_2O_2were insignificantly greater in G3 than those in G2 by 12.5 and 25.6%, respectively. This also assured the beneficial

effect of the high dose of NAC injection in reducing the OS through increasing the activity of GST and decreasing levels of MDA and H_2O_2.

It is important to clarify that, few researches have been conducted to determine the activity of GST in rabbit, most of them (Rao *et al*., 2013 and Fedets, 2015) were concerning in measuring its activity in tissues not in blood plasma or during pregnancy period. This is consistent with Fedets (2015) who found little information on GSH- dependent enzymes activity in food producing animals and stated that most of the data are about rat, mouse and human.

Regarding to the effect of gestation period, activity of GST tended to be increased with the advancement of pregnancy. It was the lowest at day 13 and the highest at kindling day. This may be to scavenge the free radicals, which produced during gestation as the embryo's weight increased. Meanwhile, levels of bothMDA and H_2O_2 were fluctuated between increases and decreases during days of pregnancy. The highest levels were recorded at day 21 for MDA and at day 13 and at kindling day for H_2O_2(Table, 1). With respect to the effect of interaction between treatment and gestation period, activity of GST rose clearly at kindling day in treated groups particularly in G3. In contrast, both MDA and H_2O_2levels were decreased in treated groups, especially in G3 (Table, 1). This, again, confirmed the beneficial influence of NAC injection in reducing the OS in pregnant rabbit does. The increase of GST activity was accompanied with the decline in both MDA and H_2O_2 levels except at day 28 of gestation. This relationship, between the three parameters (GST, MDA and H_2O_2) could be attributed to; NAC is working as intracellular GSH precursor by increasing enzymes involved in GSH synthesis. Then, the production of GSH increased which in turn increases the activity of GST to support and accelerate free radicals removal then protecting the cell against apoptosis (Lin *et al*., 1997; Eraslan *et al*., 2005 and de Andrade *et al*., 2015).

The present results agree withthose of Atef *et al*. (2016) who treated rabbitswith NAC to eliminate the toxic effect of aflatoxins and recorded that, NAC has the ability in reducing MDA and elevating GSH level. Furthermore, the present findings agree with Cam *et al*. (2008) who confirmed the safety use of NAC. They used higher doses of NAC reached to 500 mg/kg to treat rabbits from aflatoxins and they did not recorded any abnormal values in blood parameters.

1.*2. Relevant blood metabolites:*

The treatment with high or low doses of NAC did not significantly affect TP, Alb, Glb and A/G ratio and all the recorded values were close to each other

Table 1. Antioxidant status of primiparous NZW rabbit does as affected by N-acetylcysteine (NAC) administration during gestation period.

Items	GST (U/L)	MDA(nmol/L)	H_2O_2(mmol/L)
Effect of treatment (T)			
G1	1.14^{b}	4.2^{a}	4.5^{a}
G2	1.58^{ab}	3.2^{ab}	3.9^{ab}
G3	1.78^{a}	2.8^{b}	2.9^{b}
S.E	0.18	0.38	0.62
Effect of gestation days (GD)			
13	1.3	3.6	4.4
21	1.6	3.8	3.6
28	1.4	2.7	2.7
Parturition	1.7	3.3	4.4
S.E	0.21	0.44	0.71

Effect of interaction (T × GD)

	G1	G2	G3	G1	G2	G3	G1	G2	G3
13	0.9	1.5	1.4	4.2	3.5	3.3	3.8^{abc}	6.3^{a}	3.8^{bc}
21	1.0	1.8	2.1	5.1	3.2	3.0	5.7^{ab}	4.3^{abc}	3.1^{abc}
28	1.3	1.4	1.4	3.5	4.1	2.7	5.3^{ab}	5.7^{ab}	4.4^{abc}
Parturition	1.4	2.1	2.7	3.7	2.0	2.2	3.3^{abc}	2.5^{c}	2.1^{bc}
S.E	0.4	0. 4	0. 4	0.8	0.8	0.8	1.23	1.23	1.23

a, b,c Means in the same column with different superscripts are significantly different ($P<0.05$). G1= control group; G2 and G3 = groups injected with 50 and 100 mg NAC / kg body weight**.**

as shown in Table (2). The obtained values are within the normal physiological range according to Özkan *et al*. (2012) who stated that TP in female rabbits ranged between 4.9–7.9 g/dl. In addition, Verag (2002) reported that Alb level in rabbits normally ranged from 2.7 to 5.0 g/dl and from 1.5 to 2.7 g/dl for Glb. This indicate that NAC injection has no adverse effect on metabolic processes and assured the safety use of NAC. It is well known that blood proteins are good indicators of animal health, particularly Alb level which considered as a reflection of the animal ability to synthesize and store protein and working as an index of nutrition status (Ashour *etal*., 2004 and Meineri *et al*., 2016).

The present results disagree with those ofCam *et al*. (2008) who administered NAC intramuscular (250 mg/kg body weight) to treat rabbits from aflatoxin. They recorded a decrease in serum TP (decreased from 6.7 to 4.7 g/dl). Also, the study disagree withAtakisi *et al*. (2016) they treated New Zealand rabbits with NAC and collected blood samples after 3,6 and 9 hours of NAC injection and found that, TP concentration declined from 6.00 before injection to 5.5 g/dl after 9 hours of NAC injection. The same decline was found for Alb and Glb concentrations. During gestation period from day 13 to day 30, the current averages of TP, Alb, Glb concentrations and A/G ratio are 6.2, 3.7, 2.5 g/dl and 1.5, respectively. The obtained averages of TP, Alb and A/G ratio were higher than those found by Ashour *et al*. (2017) they recorded that TP, Alb and A/G in primiparious NZW rabbits were 5.65, 2.89 and 1.06 g/dl, respectively.Whereas, the present value of Glb (2.5 g/dl) is slightly lower than that (2.8 g/dl) of the later authors. These differences may be attributed to the climatic conditions, where their experiment was executed during the hottest months of summer season in Egypt. Meanwhile, the present experiment was carried out during the comfortable months for NZW in Egypt.

During gestation days, blood proteins tended to increase with the advancement of pregnancy. Values of TP, Alb and Glb increased from day 13 reaching to the highest values on kindling day by 14.6, 18.9 and 9.5%, respectively. Meanwhile, A/G ratio showed the same value during the gestation days, except on day 21, which showed the highest value (Table, 2). These increases in blood proteins with pregnancy progress might reflect the increase of both metabolic rate and liver function. Our findings are in agreement with those of Azoz and El-Kholy (2005), they found an increase in blood proteins during pregnancy in rabbits. In contrast, our findings disagree with those of Brzostowski *et al*. (1996), Ozegbe (2005) and Wahab *et al*. (2016), they found that the decreased TP during entire pregnancy period in rabbits may associated with the rapid growth rate (especially in the second half of pregnancy) of the developing fetus. Additionally, they reported that, the decline in Alb concentration might due to the increase blood volume that occurred due to hemodilution during successful pregnancy.

The interaction between treatment with NAC and days of pregnancy cleared that; values of blood proteins did not differed with the two different doses of NAC. The ratio of A/G was fluctuated between increasing and decreasing during gestation days and did not affected by NAC treatment.

Circulating TG showed opposite trend to that of blood proteins, it was affected significantly by NAC injection. Levels of TG decreased ($P<0.05$) in

treated groups (G2 and G3) than that of control group (G1) by 16.3 and 19.5%, respectively (Table, 2). The difference between the treated groups was insignificant, G3 had lower level of TG than that of G2 by 5% only. Values of TG in G2 and G3 are within the normal range as reported by Verga (2002), who found that TG normally ranged between 123.9 and 155.8 mg/dl. Level of TG in G1 exceeded slightly this range (Table, 2). The present levels of TG in treated groups are in close to that which found in rabbits (128.03 mg/dl) by Meineri *et al*. (2016). TG is the lipids storage in blood plasma, so the body can use it as a fuel under physiological adjustment (Wahab *et al*., 2016) and express exactly about the overall metabolism of nutrients. With progress of gestation days, TG levels declined gradually and insignificantly. They were decreased from the highest value on day 13 to the lowest value on kindling day by 17.2 % (Table, 2). These decreases are due to the needs of more energy to meet fetal organogenesis requirements, which increased intensively during the second half of pregnancy (Wahab *et al*., 2016). The effect of interaction between NAC injection and all the studied days was insignificant (Table, 2). This effect cleared that all levels of TG were always lower in treated groups (G2 and G3) than those in G1 during all studied days. In particular G3 which showed the lowest values of TG, whereas G1 exhibited the highest values during all days (Table, 2). Furthermore, the interaction effect revealed that TG levels decreased gradually and insignificantly with the increase of gestation days in the three groups. Level of TG declined from day 13 to kindling day by 30.7% (G1), 13.8 % (G2) and 7.1 % (G3).

This could be explained according to the results of Brizzi *et al*. (2003) and Diniz *et al*. (2006). They illustrated that, the antioxidant features of NAC may gave it the putative mechanism in reducing blood lipids and the ability to enhance cellular lipids uptake from blood. In addition, Korou *et al*. (2010)reported that NAC has a great ability in decreasing high level of saturated fat-induced triacylglycerol and cholesterol accumulation in mice liver through restoring the distributed lipid profile. Therefore, all the previous studies assured our findings in the ability of NAC in reducing blood TG to be in normal values. In addition, the present levels of G3are in close to Meineri *et al*. (2017) who found that the average of TG in rabbits was 128.03 mg/dl. However, this average is lower than the present average (141.3 mg/dl) which estimated during the second half period of pregnancy.

1.3. Kidney function:

Owing to the treatment effect, NAC injection insignificantly decreased BUN in treated groups (G2 and G3) than that in G1 by 8.6 and 13.3 %,

respectively. This may be due to the improvement of renal function in eliminating BUN from blood to be excreted in urine in treated groups. Concentration of BUN in rabbits influenced by many factors such as; dietary protein level, feed quality and feed restriction. Several authors have reported its normal range; Verga (2002) found that BUN ranged between 36.84 and 50.28 mg/dl. Meanwhile, Özkan *et al*. (2012) stated that BUN level in rabbits is ranged between 17.78 and 44.63 mg/dl. In the present study, BUN concentration in G1 and G2 were insignificantly higher than the normal values as mentioned before. Whereas, BUN level in G3 was fall within the normal range. This indicate that NAC treatment particularly with high dose (100 mg/kg BW, G3) may has the ability to reduce the elevated level of BUN. This finding agree with that of Cam *et al*. (2008) who reported that NAC provides protection against negative effects on performance, renal and liver damage and biochemical alterations induced by diseases. The present values of BUN were higher than those reported by Atef *et al*. (2016) who treated rabbits that suffered from aflatoxin, with NAC and found that BUN levels in control group was 39.48 mg/dl.

The opposite trend was obtained for CR concentration. It was increased slightly in both G2 and G3 than that of G1 by 2.3 and 5.5 %, respectively (Table, 3). Level of CR was significantly higher in G3 than that in both G1 and G2, but still within the normal physiological range according to Özkan *et al*. (2012), who found that CR concentration ranged between 0.68 – 1.58 mg/dl. This means that, NAC treatment did not negatively affect kidney function. Creatinine is the nitrogen waste product of creatine that presented in muscles. Any changes in its concentration is pointing to renal functions, for example renal diseases resulting in abnormal elevation in creatinine level. When the improvement of renal function takes place, creatinine level returns to its normal value (Verga, 2002).

Through 13-30 days of pregnancy, the present averages of both BUN and CR concentrations were 52.2 and 0.88 mg/dl, respectively. The present value of BUN is greatly higher than that (16.0 mg/dl) found by Ashour *et al*. (2017)in primiparous NZW rabbit does, meanwhile the CR level (0.88 mg/dl) is almost the same.Days of gestation had obvious effect on both BUN and CR concentrations. With advancement of gestation days, BUN level tended to decrease. It was reduced ($P<0.05$) from the highest value on day 13 to kindling day by 28.1%. However, it was insignificantly changed during the remain days and showed the lowest value on day 28 (Table 3).

Table 3. Blood urea nitrogen (BUN) and creatinine (CR) concentrations (mg/dl) ofprimiparous NZW rabbits as influenced by N-acetylecysteine (NAC) administrationduring gestation period.

Items	**BUN**			**CR**		
	Effect of treatment (T)					
G1	56.29			0.86^{b}		
G2	51.47			0.88^{b}		
G3	48.79			0.91^{a}		
S.E	2.78			0.008		
Effect of gestation days (GD)						
13	65.45^{a}			0.83^{c}		
21	51.35^{b}			0.80^{c}		
28	44.89^{b}			0.92^{b}		
Parturition	47.05^{b}			0.97^{a}		
S.E	3.21			0.009		
Average	52.2±2.1			0.88±0.01		
Effect of interaction (T × GD)						
	G1	**G2**	**G3**	**G1**	**G2**	**G3**
13	68.52	59.93	67.89	0.79^{d}	0.88^{bc}	0.81^{d}
21	58.70	46.86	48.49	0.79^{d}	0.72^{e}	0.89^{bc}
28	48.55	46.85	39.27	0.86^{c}	0.93^{ab}	0.96^{a}
Parturition	49.39	52.22	39.53	0.97^{a}	0.98^{a}	0.97^{a}
S.E	5.57	5.57	5.57	0.02	0.02	0.02

a, b,c Means in the same column with different superscripts are significantly different ($P<0.05$).G1= control group; G2 and G3 = groups injected with 50 and 100 mg NAC / kg body weight.

Contrarily, CR level tended to increase with gestation progress. It was increased from day 13 to reach the highest value on day of parturition by 16.9 %. These increases in CR level might reflect the elevated level of protein metabolism during this important period for fetal growth (Gurgoze *et al*., 2009). The effect of interaction between treatment and gestation days confirmed the previous findings that the beneficial effect of high dose of NAC in remarkable reducing (in G3) of BUN than the other two groups, in specific G1. In the three groups, the lowest values of BUN were observed on day 28 and the highest were obtained on day 13. Whereas, the highest values of CR were observed on kindling day in the three groups (Table 3). Our findings disagree with those of Wahab *et al*. (2016) who recorded a gradual decline in CR levels in pregnant rabbits during days 13, 18 and 28 of

gestation being 0.99, 0.81 and 0.79 mg/dl, respectively. They attributed this decline to the increased of glomerular filtration rate.

1.4 .Liver function:

Activities of transaminase enzymes in the three groups ranged between 21.9 and 29.8 U/L for AST and between 33.9 and 50.1 U/L for ALT (Table, 4). The present values of these enzymes are within the normal physiological ranges, which ranged from 10 to 98 U/L for AST and from 25 to 65 U/L for ALT as reported by Verga (2002). He also stated that, ALT activity in rabbits is lower than the other species. These findings indicate that, NAC treatment had no negative effect on liver function and assured the good health status of rabbits, where an elevation of these enzymes is consider a sign of liver disease (Benson and Paul-Murphy, 1999 and Jenkins, 2000). During gestation period (13-30 days), the averages of AST and ALT activities were 26.7 and 39.9 U/L, respectively. The present values disagree with those of Ashour *et al*. (2017) who found that the activities of both AST and ALT in primiparous NZW rabbits were 28.50 and 20.28 U/L, respectively.

With regard to the effect of treatment, NAC injection decreased both AST and ALT activities in treated does in comparison with those in G1 (Table, 4). AST and ALT activity decreased slightly and insignificantly in G2 than that in G1 by 4.5 and 13.8%, respectively. Meanwhile, those enzymes declined markedly and significantly in G3 than that in G1 by 26.3 and 32.3%, respectively. The remarkable decreases (above 20%) of both AST and ALT activity in G3 compared to G2 cleared that the high dose (G3) of NAC injection was more effective in reducing their levels, but still within the normal ranges, than that of the low dose (G2). This, again, assure the safety application of NAC treatment in reducing enzymes activity without harmful and complicated effects on liver function. These results confirmed by Wang *et al*. (2015) who reported that NAC could inhibit and reduce the expression of inflammatory cytokines that caused the difference in serum AST and ALT which considered to be one metric to assess severity of liver injury. It is clear that the highest activity of AST and ALT were observed in G1 and the lowest ones were obtained in G3 (Table 4).

Days of pregnancy had a marked effect on both AST and ALT activity. Both AST and ALT declined ($P<0.05$) from the highest values on day 13 to the lowest values on kindling day by 37.8 and 65.8%, respectively.

Table 4. Activities (U/L) of aspartate amino transaminase (AST) and alanine amino transaminase (ALT) in primiparous NZW rabbit does as influenced by N- acetylsysteine (NAC) administration during gestation period.

Items	**AST**			**ALT**		
Effect of treatment (T)						
G1	29.75^{a}			50.08^{a}		
G2	28.42^{a}			43.17^{b}		
G3	21.92^{b}			33.92^{c}		
S.E	1.58			2.01		
Effect of gestation days (GD)						
13	35.89^{a}			64.57^{a}		
21	22.78^{b}			42.56^{b}		
28	25.79^{b}			30.22^{c}		
Parturition	22.33^{b}			22.11^{c}		
S.E	1.83			2.32		
Effect of interaction (T × GD)						
	G1	**G2**	**G3**	**G1**	**G2**	**G3**
13	43^{a}	34^{ab}	30^{bc}	67^{a}	58^{b}	66^{c}
21	35^{bc}	26^{bc}	25^{d}	55^{c}	42^{d}	40^{de}
28	26^{cd}	30^{bc}	28^{bc}	35^{ef}	32^{ef}	34^{f}
Parturition	29^{bc}	26^{cd}	25^{d}	22^{ef}	26^{ef}	27^{ef}
S.E	3.2	3.2	3.2	4.01	4.01	4.01

a, b,c Means in the same column with different superscripts are significantly different ($P<0.05$). G1= control group; G2 and G3 = groups injected with 50 and 100 mg NAC / kg body weight.

The decline in ALT activity was more pronounced than that of AST (Table, 4). The high levels of both enzymes during all gestation days than that at parturition could be attributed to the hyper activity of liver during these days for increasing metabolism due to fetal growth. These findings are in agreement with those of Wells *et al*. (1999) and Wahab *et al*.(2016). However, the present results disagree with those of El-Mghawry *et al*. (2000), Azoz and El-Kholy (2005) and Sayed *et al*. (2005), they found an elevation in AST and ALT activity during gestation period in rabbits. Data of interaction between treatment and days of gestation cleared that, both enzymes decreased with advancement of pregnancy in the three groups from the highest values on day 13 to the lowest values at day of parturition, except G1 which showed the lowest value of AST at the day 28 of pregnancy.

2. Reproductive traits:

2.1. Doe weights:

Data in Table (5) showed that NAC administration had a positive effect on live BW of does in G3 group that injected with 100 mg/kg BW. Their BW was insignificantly increased by 1.5, 3.1 and 3.0% at the 28th day of pregnancy, at partum and at weaning days, in spite of their BW was almost equal with that of G1 group on day 14 of pregnancy (after one day of NAC injection). On the other side, injected primiparous does in G2 exhibited comparable values of BW to those in control group (G1). Their BW slightly and insignificantly decreased and increased through the respective four times (Table 5). However, the differences and changes in live BW of the three groups across the experimental period were insignificant.

The noticed numerical increase in BW of treated does in G3 could be attributed to their improvement of the physiological traits especially the antioxidant status as shown in Table (1) and animal health as confirmed by kidney andliver functions (Tables 3 and 4).

On day 14 of pregnancy, the highest BW was observed in control group followed by those in G3 then G2. As pregnancy advanced, does´ weight increased by 8.7, 13.1 and 10.9 % from day 14 through day 28 in G1, G2 and G3, respectively due to the increase in embryo weight and the presence of embryonic fluids. From day 14 of pregnancy to parturition day, does´ weight were declined in the three groups. This decline was greatest in G1 (- 4.3%), moderate in G2 (- 2.2%) and lowest in G3 (- 0.7%). It is clear that, the reduction in BW of treated does was lesser than that in control group, particularly in G3. This may be due to NAC injection helps does to sustain their BW and health as proved previously (Tables, 1, 2, 3 and 4). Meanwhile, the decline rate in does´ weight from kindling day to weaning day was slightly higher (-2.4%) in treated groups (G2 and G3) than that in G1 (-2.3%). This may be due to that treated does nursing greater size and weight of their kits than those in G1 (Table, 5). From day 14 to weaning day, the average of doe weights in G1, G2 and G3 were 3065, 3062 and 3121 g, respectively.

2.2. Litter size:

Litter size (LS) increased obviously due to NAC injection in G2 and G3 than that in G1 (Table 5 and Figs. 1 & 2). These increases in LS ranged between 19 % at birth to 35% at weaning in G3 compared to G1. Whereas, the corresponding increases in G2 were 5.5% to 23.1%. It is clear that, values of G3- G1 were always higher ($P<0.05$) than those of G2 – G1 during all the

Table 5. Body weight, litter size and weight of primiparous NZW rabbit does as influenced by N-acetylecysteine (NAC) administration.

Days	G1	G2	G3	S.E
Doe weights (g)				
14th day of pregnancy	3078	3013	3067	70.16
28th day of pregnancy	3348	3407	3400	57.03
Kindling day	2950	2948	3045	63.32
Weaning day	2885	2880	2975	62.52
Litter size (No.)				
At birth	5.67	6.00	7.00	0.38
7	5.00^{b}	6.00^{ab}	6.67^{a}	0.38
14	4.33^{b}	5.67^{ab}	6.67^{a}	0.47
21	4.33^{b}	5.33^{ab}	6.67^{a}	0.47
28	4.33^{b}	5.33^{ab}	6.67^{a}	0.47
30 (Weaning)	4.33^{a}	5.33^{ab}	6.67^{a}	0.47
Litter weights (g)				
At birth	298.33	303.33	365.00	25.64
7	561.67^{b}	715.00^{a}	740.00^{a}	36.98
14	858.33^{b}	1055.00^{ab}	1148.33^{a}	56.85
21	1238.33^{b}	1435.00^{ab}	1551.67^{a}	78.42
28	1605.00^{b}	1786.67^{ab}	1990.00^{a}	102.54
30 (Weaning)	2261.67^{b}	2816.67^{ab}	3060.00^{a}	168.44

$^{a, b}$, c Means in the same column with different superscripts are significantly different ($P<0.05$).G1= control group; G2 and G3 = groups injected with 50 and 100 mg NAC / kg body weight.

days from birth to weaning. At both 21 and 30 days, G3 and G2 had higher LS than that of G1 by 35% and 23%, respectively (Table 5 and Fig. 2).

LS was always the highest ($P<0.05$) in G3 and the lowest in G1 during all the days post-partum. During the first week of lactation, LS reduced by 11.8% and 4.7% in G1 and G3, respectively (Table, 6). In contrast, it was stabilized in G2, may be due to the higher MY in this group in comparison to the other groups (Table, 7). Thereafter, the LS was stabilized from the mid

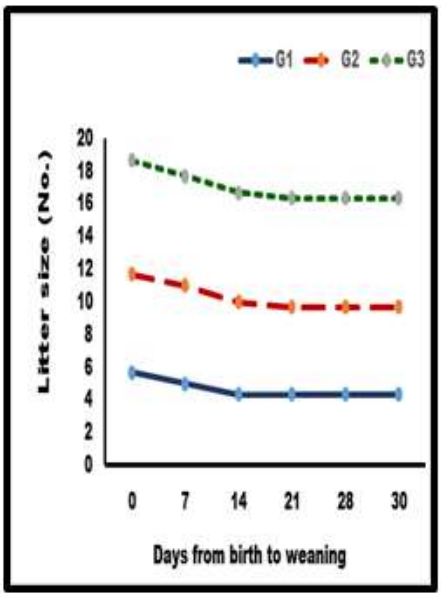

Fig. 1. Litter size from birth to weaning (30) days in control (G1) and treated (G2 and G3) does that injected with N-acetylecysteine .

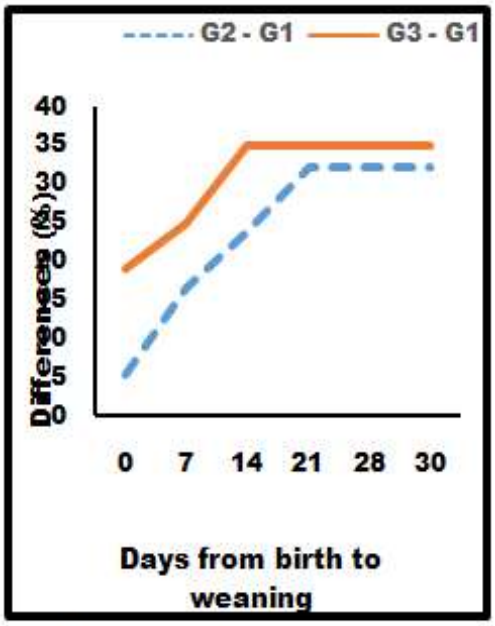

Fig. 2. Differences (%) in litter size that produced by dams injected with N- acetylecysteine

lactation to the weaning (Table 6 and Fig., 1). This observation may be due to that kits during this period depend on both mother's milk and offered feed.

During weaning period (0-30 days), the averages of LS were 4.67 in G1, 5.61 in G2 and 6.72 in G3. Averages of LS in G2 and G3 were higher than that of G1 by 20 and 44%, respectively. It is obvious that administration with NAC had a pronounced effect on mortality rate (MR). Kits of the treated does (G2 and G3) showed lower MR than those in control group. From birth to weaning, it was the highest in G1 (23.6%), followed by G2 (11.2%) and the lowest in G3 (4.7%). The improvement in reproductive traits of primiparous rabbit does in the current study could be attributed to NAC treatment which promoted the physiological traits particularly the antioxidant status and their health as proved by efficient liver and kidney functions.

Table 6. Average ofDaily (DMY) and total (TMY) milk yield (g/d) as influenced by N- Acetylecysteine (NAC) administration in primiparous NZW rabbit does during the four weeks oflactation.

Groups	DMY(Weeks)				TMY
	1	2	3	4	
G1	70.0[b]	116.7	156.7[b]	103.3[ab]	117.7[b]
G2	85.0[ab]	113.3	171.7[ab]	96.7[b]	116.7[ab]
G3	90.0[a]	128.3	188.3[a]	118.3[a]	131.3[a]
S.E	5.0	7.6	8.2	6.0	4.5

[a, b ,c] Means in the same column with different superscripts are significantly different (P<0.05).G1= control group; G2 and G3 = groups injected with 50 and 100 mg NAC / kg body weight.

2.3. ***Litter weight:***

Administration with NAC enhanced suckling kits´ weight as presented in Table (5) and Figs. (3 & 4). Their weight increased progressively form birth till weaning by 86.8, 89.2 and 88.1 % in G1, G2 and G3, respectively. The greatest increase in treated groups attributed mainly to the higher milk yield than the control group (Table, 6). Both treated groups (G2 and G3) showed heavier litter weights (LW) than those in control group (G1) during all the experimental days (Figs., 3 and 4). During the post-partum days till weaning, the increases in LW of G3 and G2 over those in G1 ranged between 18.2 to 26.1 % and 1.6 to 21.4%, respectively (Fig. 3). On day 21 and day 30, litter weights in G3 and G2 exceeded those in G1 by about 20 and 14% and 26 and 20 %, respectively. However, the difference between G2 and G3 was insignificant. Meanwhile, the changes among the three groups at birth were insignificant (Table, 5). The greatest increases in LWs were occurred during the last period (28-30 day) just before weaning. These increases were 40.9, 57.6 and 53.8% in G1, G2 and G3, respectively. It is well known that, LW at birth is the most important factor among the different factors that affecting MY. It could be noticed that kits born with heavier weight (G3) grew faster than those born with lower litter weight (G1 and G2). From the present results, the increased LW in injected groups (G3 followed by G2) with NAC than that in control group (G1) may attributed to that NAC injection caused an elevation in MY, therefore providing the sufficient quantity of milk for the growing kits.

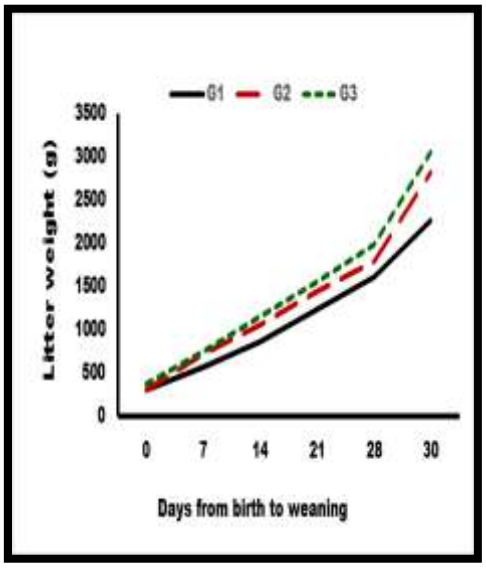

Fig. 3. Advances in litter weights from birth to weaning (30) days in control (G1) and treated (G2 and G3) does that injected with N-acetylecysteine

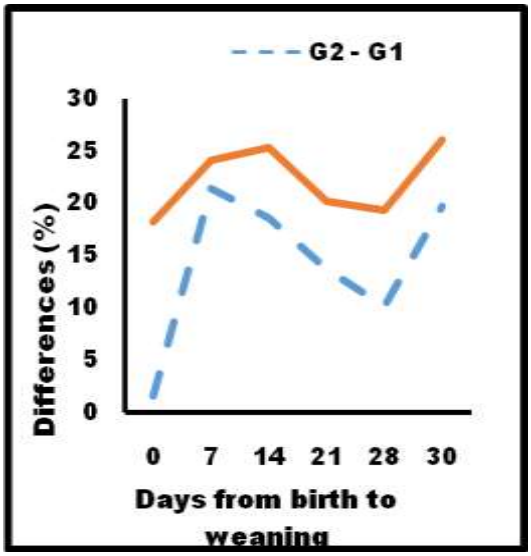

Fig. 4. Differences (%) in kits´ weight produced by dams injected with N- acetylecysteine during the post-partum period (0-30 days).

As reported in previous studies, rabbit's milk is the source of nourishment for the newborn that needs high-energy requirement. Therefore, their early ability to grow well is closely related to the quality of milk especially that are depending on their mother in feeding for 18-19 day of age (Farga *et al*., 1989; Lukefahr *et al*., 1989 and Toranto *et al*., 2003). Drummont *et al*. (2000) and chrenek *et al*. (2007) stated that rabbit pups with higher birth weight grew faster than the lower one. This explain the rapid growth of kits in G3 in comparison with G1 and reaching to the heaviest weaning weight.

3. Productive performance:

3.1. Milk yield:

Average of total milk yield (TMY, g/day) was increased significantly in G3 and insignificantly in G2 than that in G1 by 17.5 and 4.5%, respectively

(Table 6 and Fig., 5). The increased TMY in treated groups could be attributed to the increased their LS and LW, as shown previously (Table 5), in comparison to those in G1. The LS and LW are the main factors that affecting MY in rabbit does (Maertens *et al*., 2006). In addition, Partridgeand Allen (1982) found that when does are nursed 8 kits their milk production increased by 24.1% than those nursed 4 kits only. Furthermore, it could be noticed that the high dose of NAC injection was more effective in promoting milk production as seen in G3 (Table, 6). Where, does in G3 produced more milk than those in G2 that injected with low dose throughout the four lactation weeks (1,2,3 and 4) by 5.6, 11.7, 8.8 and 18.3%, respectively and also on average by 11.1%.

Moreover, this notice confirmed by the highest amounts of DMY and TMY in G3 during all lactation period (Table, 6). Also, the effect of high dose (G3) was more evident than that of low dose (G2) in comparison with G1. Where, the DMY during the consecutive four weeks of lactation in G3 were greater than those in G1 by 28.6, 9.9, 20.6 and 14.5%, respectively. Meanwhile, DMY in G2 compared to G1 was increased by 21.4 and 9.6 % in the 1st and 3rd weeks and decreased by 2.9 and 6.4 % in the 2nd and 4th weeks. These findings revealed that high dose (100 mg/kg BW) had positive impact in enhancing milk production as proved in dose of G3 which had the better antioxidant status, kidney and liver functions as shown in Tables (1, 3 and 4).The primiparous rabbits does, in the three groups, lactated for four weeks reached their peak at the third week of lactation (Fig.,5). This is agree with Casado *et al*. (2006) they stated that, lactation period in rabbit does usually ranged between 4-5 weeks; reaching their peak of lactation after 18-19 day of kindling. However, primiparous does may be subjected to intensive reproductive rhythm; their peak of lactation will be earlier 2-3 days (Pascual *et al*., 1999). In the current study, does in G1, G2 and G3 increased their DMY from the 1st wk. to the 2nd wk. by 66.7, 33.3 and 42.6%, respectively. The corresponding increases from the 2nd to the 3rd wks. were 34.3, 51.5 and 46.8%, respectively. Meanwhile, DMY dropped directly and drastically by 34.1, 43.7 and 37.2%, respectively, during the last week of lactation. Thus, the three groups showed the same pattern of milk production during the whole period of lactation. Our findings are fully agree with those of Lukafahr *et al*. (1983), Cherenk *et al*. (2007) and El-Sabrout *et al*. (2017), they reported that, rabbits milk is elevating gradually until the day 20 of lactation, afterwards it is declined reaching to the end of lactation (generally at day 30 of lactation).

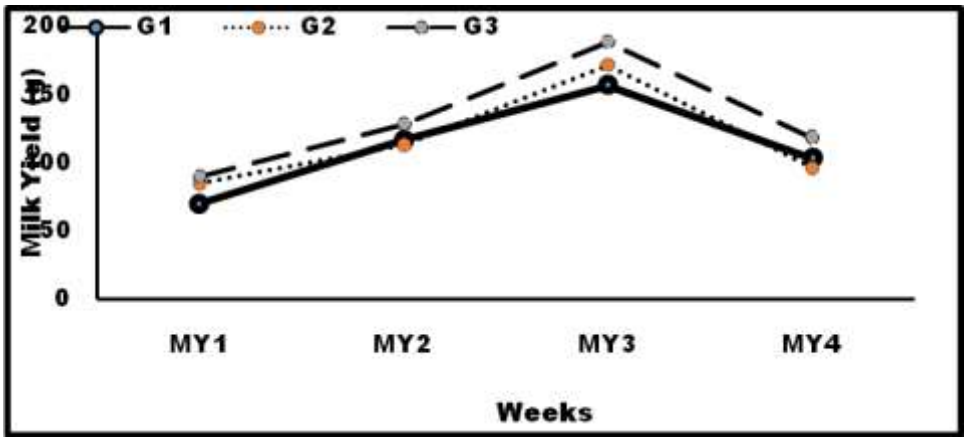

Fig. 5. Daily milk yield (DMY, g/d) as influenced by NAC administration in primiparous NZW rabbit does during the four weeks of lactation.

3.2. Milk compositions:

The effect of NAC administration was insignificant on all milk components, except ML (Table 7). MF (%) insignificantly decreased in G2 and G3 compared to G1 by 12.3 % and 16.4 %, respectively. This attributed mainly to the higher MY in treated groups than that in control group. It is well established that there was inverse relationship between MY and MF (%). In the three groups, values of MP (%) were almost constant. However, MP (%) was slightly and insignificantly lower in G2 and G3 by 3.6 and 1.8 % than those in G1. In comparison with G1, ML (%) increased ($P<0.05$) in G3 by 15.2 % and decreased insignificantly in G2 by 7.4 %. Ash content (%) of rabbits' milk was equal in the three groups. Whereas, MTS (%) was decreased slightly in G2 and G3 by 6.2 and 5.1 % compared to G1. MSNF (%) was equal in G3 and G1 and decreased slightly in G2 by 3.4% than that of G1.

During lactation weeks, MF (%) showed the highest value at the 1stwk, then dropped ($P<0.05$) markedly during the 2nd and 3rd wks, to reach the lowest value at the 3rdwk (peak of lactation) by 49.1 % and increased ($P<0.05$) at the end of lactation (Table 7). Maertens *et al.*(2006) reviewed that the fat content of doe milk during the 4wks of lactation period ranged between 12.7 % in wk 1 and 14.0 % in wk 4, with an average of 12.9 %. This average is higher than the present average (11.0%). Meanwhile, MP (%) increased ($P<0.05$) gradually with the increase of lactation wks., except at the

Table 7. Impact of N-acetylcysteine (NAC) administrations on milk compositions (%)in primiparous NZW rabbit does.

Groups	MF	MP	ML	Ash	MTS	MSNF
Effect of treatment						
G1	12.2	16.9	2.82^{b}	7.01	39.0	26.78
G2	10.7	16.3	2.61^{b}	7.03	36.6	25.88
G3	10.2	16.6	3.25^{a}	7.02	37.0	26.83
S.E	0.71	0.38	0.11	0.02	0.92	0.41
Weeks of lactation period						
1	14.8^{a}	15.1^{b}	1.68^{c}	7.00	38.6^{b}	23.8^{c}
2	8.42^{b}	17.4^{a}	3.22^{ab}	7.03	36.1^{bc}	27.7^{a}
3	7.54^{b}	15.5^{b}	3.57^{a}	7.04	33.7^{c}	26.1^{b}
4	13.2^{a}	18.4^{a}	3.10^{b}	7.00	41.7^{a}	28.5^{a}
S.E	0.82	0.44	0.13	0.02	1.06	0.47

$^{a, b, c}$ Means in the same column with different superscripts are significantly different ($P<0.05$). G1= control group G2 and G3 = groups injected with 50 and 100 mg NAC / kg body weight.

3rdwk. It was increased ($P<0.05$) from the lowest value at the 1stwk to the highest value at the 4thwkby 22 %. This result is comparable to that reported by Peaker and Taylor(1975) they found that MP was increased during the whole lactation period. In contrast, the present values of MP are much higher during all lactation stage than those reported by Maertens *et al.*(2006) who stated that the MP content during the entire lactation period (4 wks) ranged between 11.9% in wk 3 and 13.4% in wk 4, with an average of 12.3 %. This average is more lower than the present average (16.6 %).

ML (%) increased sharply during the first three wks of lactation. It was rose ($P<0.05$) from the lowest value at the 1stwk to the highest value at the 3rd wk by 112.5%. Then, slightly declined at the 4thwk (Table, 7). These results agree with those of Peaker and Taylor (1975). But, disagree with those of Maertens *et al.*(2006) who reviewed that ML declined by the ending of lactation and the amount of decreasing in ML was higher than drop in MY. In addition, the present value of ML during the 2nd, 3rd and 4th wks were more greater than those of Maertens *et al.*(2006) who stated that the ML of doe milk ranged between 1.6% (1st wk) and 1.9% (3rd wk) during the 4 wks of

lactation, with an average of 1.7%. The present average (2.9%) of ML is striking higher than that average. It is well known that the lactose and sodium are two of the main constituents concerned in maintaining the constancy of the osmotic properties of milk (Maertens *et al*.,2006).

Milk ash (%) was stable throughout the whole lactation period. This finding is completely disagree with that of Maertens *el al.*(2006) who stated that the ash content of rabbit milk increases from about 1.9 % during the 1st wk of lactation till 2.4 % in the 4th wk of lactation. These values are strikingly more lower than the present values during all lactation stages. MTS (%) showed the same pattern of MFduring the first three weeks of lactation, it was reduced gradually. Thereafter, it was increased ($P<0.05$) from the lowest value at the 3rd wk to the highest value at the 4th wk by 24%. Moreover, MSNF (%) changed ($P<0.05$) during the first three wks. of lactation, then increased ($P<0.05$) during the last wk. It was elevated ($P<0.05$) from the first to the last wk by 20%. The present average of MTS and MSNF were 37.5 and 26.5 %, respectively.

In general, milk composition (%) of MP, ML, MTS and MSNF significantly increased from the first wk. to the last wk. of lactation. Whereas, MF insignificantly decreased and ash was constant (Table 7).

CONCLUSION

From the above mentioned results, it can be concluded that NAC injections having largest impact on rabbits performance, particularly with high dose (100 mg/kg BW).The positive and beneficial effect of NAC treatment on primiparous NZW rabbit does was very clear as confirmed by relieving the oxidative stress that results from pregnancy. It increases GST and decreases both MDA and H_2O_2. Furthermore, it reduced TG, BUN, AST and ALT indicating good health and no adverse effects on kidney and liver functions. Also, no detrimental effect on the blood parameters was observed.

From the economic point of view, NAC injection improved doe weight, increased both litter size and weight alongside reducing mortality rate. The most obvious economical effect of NAC treatment is promoting milk production especially with high doses (G3) with no detrimental effect on milk compositions, except milk lactose.

In conclusion, this study proved not only the effectiveness, but also the safety of NAC application and its capability to improve rabbit's performance. However, further studies on large numbers of rabbits and for many parities are urgently needed to confirm our findings.

REFERENCES

Agostinis, C.; Zorzet, S.; De Leo, R.; Zauli, G.; De Seta, F. and Bulla, R. (2014). The combination of N-Acetylcysteine, Alpha-Lipoic Acid, and Bromelain shows high anti-inflammatory properties in novel In vivo and In vitro models of endometriosis. *J. Media. Inflamm*., 3: 1-9.

Ashour, G.; Ibrahim, S. A.; Ismail, A. M. and El-Kholy, K. H. (2004). Physiological reactions and biological performance of rabbits to summer heat stress. *2nd Sci. Conf. on Physiol. Resp. to Environ*. Cond., 28-31 July, 2004, El-Arish, Egypt, pp. 165-186.

Ashour, G.; Sedki, A.A.; Abdel-Rahman Samah, M. and. El-Kholy, K. H. (2017). Physiological responses of rabbit does to Synertox® supplementation under different housing conditions during summer in Egypt. *Egypt. J. Rabbit Sci*., 27: 377- 397.

Atakisi, E.; Birkan, T., Kezban, Canan, C.G. and Onur, A. (2016). Acute effects of N-Acetylcysteine on total antioxidant capacity, total oxidant capacity, nitric oxide level and gammaglutamyl transpeptidase activity in rabbits.Kafkas Univ. Vet. Fak. Derg., 22:871-875.

Atef, H.A.; Mansour Mogda K.; Essam, M. I.;Darwish, A. S., Al-Kalamawy, N.M; Ali,M. A. and Flourage, M.R. (2016). Aflatoxicosis in rabbits with particular reference to its control by N. acetylcysteine and probiotics. Inte. J. Current Res., 08: 22548-22560.

Azoz, A.A. and El-Kholy, K. H. (2005). Blood metabolites and hormones of V-line and Bauscat female rabbits under middle Egypt conditions.Egypt. J. Rabbit Sci., 15: 131- 142.

Benson, K.G. and Paul-Murphy, J. (1999). Clinical Pathology of the Domestic Rabbit. Vet. Clin. Exotic. Anim. Pract., 2: 539–552.

Brizzi, P.; Tonolo, G.; Carusillo. F.; Malaguarnera, M.; Maioli, M. and Musumeci, S. **(2003).** Plasma lipid composition and LDL oxidation. Clin. Chem. Lab. Med., 41:56-60.

Brzostowski, H.; Milewski, S.; Wasilewska, A. and Tanski, Z.(1996). The influence of the reproductive cycle on levels of some metabolism indices in ewes. *Arch. Vet. Polonic*.,35:53–62.

Çam, Y.; Eraslan, G.; Atasever, A.; Eren, M.; Liman, B.C. and Şeybek, N. (2008). Efficacy of N-Acetylcysteine on aflatoxicosis in rabbits. *Polish J. Environ. Stud*., 17: 189-197.

Casado, C.; Piquer, O.; Cervera, C. and Pascual, J.J. (2006). Modelling the lactation curve of rabbit does: Towards a model including fit suitability and biological interpretation. *Livest. Prod. Sci.*, 99: 39-49.

Chrenek, P.; Chrastinova,L.; Kirchnerova, K.; Makarevich, A. V. and Foltys, V. (2007). The yield and composition of milk from transgenic rabbits. *Asian-Aust. J. Anim. Sci.*, 20: 482 – 486.

Diab, R.A.; El Sehemy, M.M.; Mohamed, N.E.; Salim, F. and Hussein, A.Z. (2003). Enterotoxaemia in rabbits and trials for preparing vaccine from the isolated strains. *J. Egypt. Vet. Med. Assoc.*, 2: 59-64.

de Andrade, K.Q.; Fabiana, A.M.; John,M.D.; Orlando, R.P.; de Farias,J.C. and Marília, M.O.F. (2015).A review, Oxidative Stress and Inflammation inHepatic Diseases: Therapeutic Possibilitiesof N-Acetylcysteine. *Inter. J. Mol. Sci.*, 16: 30269–30308.

Duncan, D. E. (1955). Multiple range and Multiple F test. Biometrics, 11: 1-42.

Diniz, Y.S.; Rocha, K.K.; Souza, G.A.; Galhardi, C.M.,; Ebaid, G.M.; Rodrigues, H.G.; Novelli Filho, J.L.; Cicogna, A.C. and Novelli, E.L.(2006). Effects of N-acetylcysteine on sucrose-rich diet-induced hyperglycaemia, dyslipidemia and oxidative stress in rats. *Eur. J. Pharmacol.,* 543:151-157.

Drummond, H.; Vazquez, E.; Sanchez-Colon, S.; Martinez-Gomez, M. and Hudson, R. (2000). Competition for milk in the domestic rabbit: Survivors benefit from littermate deaths. *Ethol.*, 106:511-526.

El-Maghawry, A. M.; Soliman, M. M.; El-Sayiad, GH. A. and Mahrose, KH. M. (2000). Effects of breed, season of kindling and pregnancy status on some blood measurements of doe rabbits raised in Egypt. *Egypt. J. Rabbit Sci.*, 10: 295-306.

El-Sabrout, K.; Aggag, S. and El-Raffa, A. (2017). Comparison of milk production and milk composition for an exotic and a local synthetic rabbit lines**.** *www.veterinaryworld.org/Vol.10/May-2017/10.pdf*.

Eraslan, G.; Yucel, C.; Eren, M; Camliman, B.; Atalay, O. and Seybek, N. (2005). Aspects of using N-acetyl cysteine in alflatoxicosis and its evaluation regarding some lipid peroxidation in rabbits. *Bull. Vet. Inst. Pulway.*, 49: 243 – 247.

Fedets, O. (2015). Comparison of activities of glutathione enzymes in ceacum and liver of cattle, horse, pig, rabbit and sheep. *Bulgarian Agric. Sci.*, 21:698-702

Fekete, S. and Huszenicza, G. (1993). Effects of T-2 toxin on ovarian activity and some metabolic variables of rabbits. *Lab Anim. Sci.*, 43: 646–649.

Fraga, M. J.; Lorente, M.; Carabano, R. M. and De Blas, J. C. (1989). Effect of diet and of remaining interval on milk production and milk composition of the doe rabbit. *Anim. Prod*., 48:459-465.

Gao, W.; Jin-Xiao L.; Chi M.; Jing-yin D. and Qiu, Y. (2017). The Protective effect of N-acetylcysteine on ionizing radiation induced ovarian failure and loss of ovarian reserve in female mouse. *Bio Med Res. Inter*., 1-11.

Gurgoze, S.Y.; Zonturlu, A.K.; Ozyurtlu, N. and Icen, H.(2009). Investigation of some biochemical parameters and mineral substance during pregnancy and postpartumperiod in Awassi ewes**.** *Kafkas Univ. Vet. Fakül. Derg.*, **15** : 957-963.

Hassan, F. A.M.; Mahmoud, R and El-Araby, I. (2017). Growth performance, serum biochemical, economic evaluation and IL6 gene expression in growing rabbits fed diets supplemented with zinc nanoparticles. *Zagazig Vet. J.*, 45: 238-249.

Hope, W.; Dalton, C.; Machlin, L.; Filipski, R., and Vane, F. (1975). Influence of dietary vitamin E on progstaglandine biosynthesis in rat blood. *Prostaglan*., 10: 557-571.

Jenkins, J.R. (2000). Rabbit and ferret liver and gastrointestinal testing. In: Laboratory Medicine. Avian and Exotic Pets (Fudge,A.M., ed.) W.B. Saunders, pp 291–304.

Kamboj, S.S.; Vasishta, R. K. and Sandhir, R. (2010). N-acetylecysteine inhibits hyperglycemia – induced oxidative stress and apoptosis marker in diabetic neuropathy. *J. Neurochem*., 112: 77 – 91.

Korou, L.; George, A.; Alkisti, P.; Ioannis, S. V.; Dimitrios, I.; Theodoros, K. and Despoina, N. P. (2010). Comparative antilipidemic effect of N-acetylcysteine and sesame oil administration in diet-induced hypercholesterolemic mice. *Lipids Healt. Disea*., 9:23 - 33.

Krieger, T. and Loch-Caruso, R. (2001). Antioxidants prevent V-hexachlorocyclohexane-induced inhibition of rat myometrial gap junction and contractions. *Bio. Reprod.*, 64: 537-547.

Lin C.C. and Yin, M.C. (2008). Effects of cysteine-containing compounds on biosynthesis of triacylglycerol and cholesterol and anti-oxidative protection in liver from mice consuming a high-fat diet. *Br. J. Nutr*., 99:37-43.

Lukefahr, S.; Hohenboken, W. D.; Cheeke, P. R. and Patton, N. M. (1983). Doe reproduction and preweaning litter performance of straightbred and crossbred rabbits. *J. Anim. Sci*., 57:1090-1096.

Maertens, L.; Lebas, F. and Szendrö, Zs. (2006). Rabbit milk: A review of quantity, quality and non-dietary affecting factors. *World Rabbit Sci*., 14: 205-230

Meineri, G.; Mario, G. and Gilberto, F. (2017). Evaluation of physiological parameters of the plasma oxidative status in rabbits. *J. Appl. Anim. Res*., 45: 315–319.

Mohammed, H.A.; Eid, A.A.M. and El-Bakrey, R.M.M. (2013). A review of rabbit diseases in Egypt. *J. WARTAZO*, 23: 185-194.

NRC (1977). National Research Council**.** *Nutrient Requirements of Rabbits*. Subcommittee on Rabbit Nutrition, Committee on Animal Nutrition. Board on Agriculture and Renewable Resources. National Academy of Sciences, Washington, DC, USA.

Omar, H. M., Saad El-dien, H. M.; Saeed, M. A.; Al-Salahy, M. B. and Abel-Tawab H. S.(2012). Alpha-lipoic acid and N-acetyl cysteine ameliorates oxidative stress and hepatic injury in alloxan-induced diabetic Rabbits. *Inter. J. Diabetes Res*., 1: 7-17.

Ozegbe, P.C. (2005). Comparative biochemical assessment of the amniotic fluid and maternal plasma of pregnant rabbits.Vet. Arch., **75:** 431-437.

Özkan, C.; Kaya, A. and Akgül, Y. (2012). Normal values of haematological and some biochemical parameters in serum and urine of New Zealand White rabbits. World Rabbit Sci., 20: 253 – 259.

Partridge, G.G. and Allen, S.J.(1982). The effects of different intakes of crude protein on nitrogen utilization in the pregnant and lactating rabbit. *Anim. Prod.*, 35: 145-155.

Pascual, J.J.; Tolosa, C.; Cervera, C.; Blas, E. and Fernández-Carmona, J. (1999). Effect of diets with different digestible energy content on the performance of rabbit does. Anim. Feed Sci. Technol., 81: 105-117.

Peaker, M. and Taylor, J.C. (1975). Milk secretion in the rabbit: changes during lactation and the mechanism of iron transport. *J. Physiol.,* 253: 527-545.

Rao, K. S.; Pradeepkiran, J.A.; Praveen chakravarthi, V. and Bhaskar, M. (2013). Effect of cadmium on antioxidant metabolic modulations in heart and muscle of female rabbits. Res. Artic. Biol. Sci., 3: 409-415.

Rosenthal, K. (1997) Interpretation of selected clinical pathology values in ferrets and rabbits. *Proceedings of Atlantic Coast Veterinary Conference*, 1–3.

SAS. (1999). SAS users guide. *Statistical Analysis System Institute,* Inc., Cary, NC, USA.

Sayed, M. A. M.; Azoz, A. A.; El-Mekass, A. A. and Abdel-Khalek, A. M. (2005). Some performance aspects of Bauscat doe rabbits as affected by dietary supplementation with fenugreek and aniseed. *2nd Sci. Conf. on Animal Prod.*, 27-29 September, Sakha, Kafr El-Sheikh, Egypt.

Schaefer, C.; Peters, P. and Miller, R. K. (2007). Drugs During Pregnancy and Lactation. Academic Press, Elsevier, New York, USA, 886p.

Sekine, S.; Terada, S. and Aoyama, T. (2013). Medium-chain triacylglycerol suppresses the decrease of plasma albumin level through the insulin-AktmTOR pathway in the livers of malnourished rats. *J. Nutr. Sci. Vitaminol.*, 59:123–128.

Taranto, S.; Di Meo, C.; Stanco, G.; Piccolo, G.; Gazaneo, M. P. and Nizza, A. (2003). Influence of age at weaning on caecal content characteristics and post-weaning performance and health of rabbits. *Asian-Aust. J. Anim. Sci.*, 16:1540-1544.

Verga, M. (2002). Clinical pathology. In: *Rabbit Medicine* (1st ed.). Linacre House, Jordan Hill, Oxford Ox2 8DP., pp. 140 – 164.

Wahab, A.; Hamayun, K.; Shakoor, A.; Muhammad, S. Q.; Younas, M.; Sirzamin, K.; Umar, S. and Muhammad, K. S. (2016). Biochemical profile of local rabbits (Oryctolagus cuniculus) during successful pregnancy under backyard production system. *Pakistan J. Zool*., 48: 625-630.

Wang, C.; Xia,Y.; Zheng, Y.; Dai, W.; Wang, E. Chen, K.; Li, J.; Li, S. and Zhu, R. (2015). Protective effects of N-acetylcysteine in concanavalin a-induced hepatitis in Mice. *J. Media. Inflamm*., 2:1-17.

Wells, M.Y.; Decobecq, C.P.; Decouvelaere, D.M.; Justice, C. and Guttin, P. (1999). Changes in clinical pathology parameters during gestation in the New Zealand White rabbit. *Toxicol. Pathol*., 27:370–379.

الأداء الفسيولوجي التناسلي والإنتاجي لإناث الأرانب المتأثرة بالمعاملة بالأستيل سستين

جمال عاشور حسن[١]، سماح عبد الرحمن[٢]، وائل عوض[٢]، نهي محمود عبد العظيم [٢]، صفاء عطايا بركات[٢]

١- قسم الإنتاج الحيواني -كلية زراعة - جامعة القاهرة - جيزة – مصر.

٢- معهد بحوث الإنتاج الحيواني – مركز البحوث الزراعية - جيزة – مصر.

تم إجراء هذه الدراسة في وحدة الأرانب التابعة لمحطة بحوث سخا – محافظة كفر الشيخ، ولذلك لدراسة تأثير الحقن بمركب الأستيل سستين (N-acetylcysteine, NAC) علي الخصائص الفسيولوجية والأداء التناسلي والإنتاجي لإناث الأرانب النيوزيلاندي. حيث تم إستخدام عدد ٢١ من أمهات الأرانب النيوزيلاندي

(موسم أول)تراوحت أعمارها ما بين ٥ الي ٦ شهور ومتوسط أوزانها ٣٠٥٢ جم. تم تقسيمهم إلي ثلاثة مجاميع متساوية، المجموعة الأولي هي المجموعة الكنترول (لم يتم حقنها بالمركب)، أما المجموعتين الثانية والثالثة تم حقنها تحت الجلد بمركب الأستيل سستين بمعدل ٥٠ و ١٠٠ مجم NAC/ كجم وزن حي، علي التوالي. كانت بداية الحقن بالمركب في اليوم الرابع عشر من الحمل والذي استمر لمدة سبعة أيام متتالية ، والتجربة استمرت لمدة ثلاثة شهور.

أوضحت النتائج أن الحقن بمركب الأسيتيل سستين أدي إلي خفض الإجهاد التأكسدي في المجموعتان المعاملة بالمركب مقارنة بالكنترول، حيث إزداد نشاط إنزيم GST وقابله إنخفاض في تركيز كلا من MDA و H_2O_2. كما وجد أنكلا من البروتينات الكلية ، الألبيومين، الجلوبيولين، والنسبة بين الأبيومين والجلوبيولين لم تتأثر معنويا بحقن المركب المذكور. علي العكس أظهرت الجلسريدات الثلاثية انخفاضاً (ولكن كانت في ظل المعدل الطبيعي لها) في تركيزها في المجموعات المعاملة بمركب NAC وكذلك إنخفضت بتقدم الحمل. كذلك أظهرت المجموعات المعاملة إنخفاضاً في مستوي يوريا الدم (BUN) وحدوث زيادة الكرياتنين مقارنة بمجموعة الكنترول. وكذلك أظهرت إنزيمات الكبد (ALT, AST) إنخفاضا في المجموعات المعاملة وكذلك بتقدم الحملواقتراب ميعاد الولادة.

أما بالنسبة للتغيرات في أوزان الأمهات لم تكن معنوية خلال فترة التجربة ولكن كانمن أهم النتائج هو حدوث زيادة في أوزان وأعداد الخلفات في المجموعات المعاملة بالأستيل سستين عن مجموعة الكنترول. كذلكأدت المعاملة بـ NAC إلي إنخفاض معدلات النفوق في المجموعات المعاملة بالمركب مقارنة بالكنترول ، حيث كان أقل معدل في المجموعة الثالثة (٤.٧%) وفي المجموعة الثانية ١١.٢% بينما سجلت مجموعة الكنترول معدل نفوق أعلي والذي كان ٢٣.٦%. أيضاً كان هناك زيادة ملحوظة في كمية اللبن المنتجة والتي زادت بمقدار ١٧.٥% و ٤.٥ % في المجموعات الثالثة والثانية علي التوالي مقارنة بالكنترول. اما مكونات اللبن المختلفة لم تتأثر معنوياً بالحقن فيما عدا اللاكتوز كما ان دهن اللبن إنخفض في المجموعات المعاملة عن المجموعة الكنترول .

التوصية: من نتائج هذه الداسة أظهرت مدي فاعلية وكفاءة وأمان مركب الأستيل سستين في تحسين الأداء الفسيولوجي والتناسلي والإنتاجي لإناث الأرانب وانه بحاجة الي مزيد من الدراسات تجري عليعدد أكبر من الإناث ولعدة مواسم .

الكلمات الدالة: الأرانب، الأسيتيل سستين، دلائل الإجهاد التاكسدي، نواتج التمثيل ، وظائف الكلية والكبد، عدد ووزن الخلفات، نسبة النفوق، كمية اللبن ومكوناته.