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Swayback Disease of Lambs in Basra Governorate, Iraq

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SWAYBACK disease of young lambs in Basra governorate, Iraq has been detected and diagnosed. Sixty-four local breeds lambs, a week to three months old of both sexes show various clinical manifestations of in-coordination and ataxia. Ten clinically healthy local breeds lambs were used as controls. All animals were subjected to complete clinical examinations. Diseased lambs showed different clinical signs such as, lack of coordination with ataxia in hind legs, unable to suck their dams, loss of body weight and apathy, difficulty in standing from lying down, frequent falls and permanent lying down position. The results concerning the hematological data indicate Anormocytic normochromic type of anemia with no changes in total and differential leukocytes count. Moreover, biochemical analysis of affected lambs, and controls indicated a significant decrease in copper compared with controls. Furthermore, a significant increase was detected in ALT, AST and CPK in diseased lambs compared to controls. Histopathological changes of the sciatic nerve of diseased lambs indicated marked edematous fluid in the neural interstia, as well as a marked area of vacuolated neural cells with severe congestion of blood vessels, and an obvious area of vacuolated neural cells. On the other hand, severe perivascular edema in addition to perineural edema was also detected in the brain.

Keywords: *Swayback disease, Copper deficiency, Lambs, Iraq.*

Introduction

Swayback disease (SD) (*Enzootic ataxia)* is defined as " a progressive neuropathy of young copper-deficient lambs." SD causes very significant economic losses in the farming of ruminant animals [1].It affects newborn or young lambs even from seemingly disease-free mothers. Infection occurs regardless of sex, single lambs, twins, or even all three of triplets may not escape infection. SD infection is not predisposed to an of these. It is rare for just one of twin lambs to be affected , however it has been found that in the majority of such cases, the unaffected twin develops SD later [2]. In most outbreaks, most cases are evident at birth, although in a number of cases no symptoms are manifested (or perhaps not noticed) until some weeks later. Regardless of whether the lamb is born with SD or is affected later, the symptoms manifested are basically similar [3].

Copper as a mineral and a basic micro trace element that involved in several animal organism functions. It has a significant role in the active center of twenty metalloenzymes or may be more cofactors, and metalloproteins that are linked to free devastation radicals, synthesizing of connective tissues, myelin and forming of bones, pigmentation and wool formation. It also has an indirect role in hematopoiesis [4].

Both primary deficiency copper (PDC) and secondary deficiency of copper (SDC) could cause SD as PDC is referred to as "a deficiency of copper in the diet." The most likely cause of PDC is soil that is deficient in copper in which various types of forage are grown that the animals consume. However, the "secondary deficiency of copper" (SDC) is " the disruption of the absorption of copper in the digestive system due to different reasons including the interaction between copper, molybdenum, and sulfur." The

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bonding of these three elements b leads to the formation of copper thiomolybdate, which prevents copper from being absorbed [5].

A characteristic of SD is lameness in animals, in particular in lambs and kids because of a lack of hind limb coordination. Furthermore, other signs could also be manifested such as paralysis besides incoordination of hind limbs, loss of vision and hearing, anemia and falling prostrate. Moreover, risk factors for copper deficiency include age, breed, species, physiological status and animal body reserves of copper [1,2].

It has been shown that the PDC occurs more commonly in young animals than in adults, while it is believed that the major cause of copper deficiency in younger ages is the mother animal's low copper level as well as its low secretion in the milk. However, animal breed and species could also affect the animal copper levels [4].

In SD, there is invariably ataxia, occasionally and loss of vision. SD follows a progressive non-febrile course and normally culminates in death, with the exception of the very mild cases. The highly-affected lambs die as they are unable to keep up with and suckle their dam and also from other malnutrition and secondary infections [6].

It has been documented that incorrect synthesizing of the myelin sheath may take place in mid time of gestation in fetal life, Moreover, high copper deficiencies might result in " cerebro spinal swayback," which is a congenitally based. Furthermore, newborn lambs are frail, and therefore are unable to suckle. Additionally, cavitation and softening of the white matter in the cerebrum was also observed [7].

SD *(Enzootic ataxia)* had been suspected in lambs in Basrah governorate. As such, the objective of the present investigation was to carry out clinical, hematological and diagnostic studies of this disease in Basrah, Iraq.

Materials and Methods

Animals and study design

Suspected animals were reared in the Al-Zuber district of Basrah governorate, Iraq. Selected were 64 local breed lambs, one week to three months old and of both sexes, that showed clinical signs of incoordination and ataxia, walking difficulty, frequently falling, tremors, and poor growth, Following the emergence of the symptoms, the condition deteriorated, with apathy, weight loss, and ultimate demise. A total of 19 clinically healthy local breed lambs were used as controls. All animals were subjected to complete clinical examinations, but fecal samples were screened for parasitic load, if any, using standard routine laboratory methods.

Collecting blood samples

Blood samples (10 mL) were drawn from punctures to the external jugular vein and stored in tubes that contained or did not contain the anticoagulant EDTA to obtain serum and plasma, which were kept in plastic tubes and stored at -20◦C, for later biochemical and mineral analysis. Whole blood samples (with EDTA) were utilized for the evaluation of total erythrocytic count (TRBc), hemoglobin strength (HB), packed cell volume (PCV), and total leukocytic count (TLC) (Beckman, USA), Moreover, MCV and MCHC were also extracted. Differential leukocyte count was carried out employing Giemsa stain blood smears following Weiss and Wardrop [8].

Assessment of copper

Plasma copper concentration was assessed employing the Flame atomic absorption spectrophotometer(FAAS) adopting to the approach mentioned by Xueping and Reny (2002), [9].

Assessing the copper in tissues was carried out following Akinloye et al. [10], after collection of both liver and kidney samples.

Biochemical analysis

Biochemical analysis of diseased animals serum includes estimation of ALT, AST, CPK (Spectrophotometer method employing commercial kits, Roche Diagnostics, Indianapolis, GMBH, Germany).

Histopathology analysis

Diseased lambs which die or have been slaughtered after owner approval, were subjected to histopathological examinations. Tissue samples were collected from the brain, and sciatic nerve, fixed at 10% neutral buffered formalin solution for 72 h, followed by trimming and washing and then drying before cleaning in xylol. Finally, the samples were set in paraffin wax, and divided into sections of 4-5 µ thickness. The staining of the samples was then done with hematoxyline and eosin, and scrutinized under a light microscope [11].

Statistical analysis

Analysis of statistics was performed according to Leech et al. [12]. employing student *t*.test.

Results

SD affected animals exhibit different clinical manifestations such as, lack of coordination with ataxia in hind legs (38.4%), Fig. 1, inability to suck their dams (35.2%), Loss of body weight and apathy (33.92%), difficulty in standing from a prone position (28.16%), Fig. 2, frequent falls (26.88%), and permanently lying down (7.68%). Table 1.

The hematological data results indicate that diseased animals show Normocytic normochromic type of anemia with no changes in total and differential type of leukocytes (Table.2).

Moreover, biochemical analysis of diseased lambs and controls indicated a substantial reduction ($P<0.05$).in copper in serum, liver and kidneys compared to controls, Furthermore, a substantial rise ($P<0.05$) was detected in ALT, AST and CPK in diseased lambs compared to controls . (Tables 3 and 4).

Gross scrutiny of the brain of affected lambs reveals severe congestion of the brain (Fig. 3).

Histopathological changes in the sciatic nerve of diseased lambs indicated marked edematous fluid in the neural interstia, as well as a marked area of vacuolated neural cells, with severe congestion of blood vessels. Therer was also an obvious area of vacuolated neural cells (Fig. 4 & 5). Furthermore, severe perivascular edema in addition to perineural edema was also detected in the brain (Fig. 6).

Fig. 1. Lack of coordination with ataxia in hind legs.

Fig. 2. Difficulty in standing from prone position.

TABLE 1. Clinical symptoms of diseased lambs with Swayback disease.

Clinical manifestations	Number of diseased animals n= 64	%
Lack of coordination with ataxia in hind legs	60	38.4
Unable to suck their dams	55	35.2
Loss of body weight and apathy	53	33.92
Difficult to stand from a prone position	44	28.16
Frequent falls	42	26.88
Permanent lying down position	12	7.68

TABLE 2. Hematological parameters of affected lambs with Swayback disease and controls.

Parameters	Controls *n*= 10	Diseased lambs *n*=64
RBC $\times 10^6$	7.86±1.33	5.88±0.36*
Hb g/dl	13.21 ± 1.79	10.2±0.7*
PCV %	32.55 ± 4.73	24.91±1.08*
MCV	41.42±3.24	42.36±2.43
MCHC	40.58±2.51	40.94±1.38
TLC $\times 10^3$	12.13±1.56	12.24±0.72

*Values are the mean ± standard error of mean. * (P<0.05).*

TABLE 3. Biochemical analysis of diseased lambs with Swayback disease and controls.

Parameters	Controls n= 10	Diseased lambs n=64
Copper / serum	41.6±7.27	28.12± 4.67*
ALT	33.65± 7.12	87.67±8.32*
AST	105.45± 8.81	123.33±23.55*
CPK	126.43± 5.57	188.21±12.3*

*Values are the mean ± standard error of mean. * (P<0.05).*

TABLE 4. Copper intensities in liver and kidneys of lambs affected by Swayback disease and controls.

Parameters	Controls n= 10	Diseased lambs *n*= 64
Liver Cu µmol/kg	2473±18.86	1963±13.11*
Kidney Cu µmol/kg	253.11±48.25	188.46±6.7*

*Values are the mean ± standard error of mean. ** (P<0.05).*

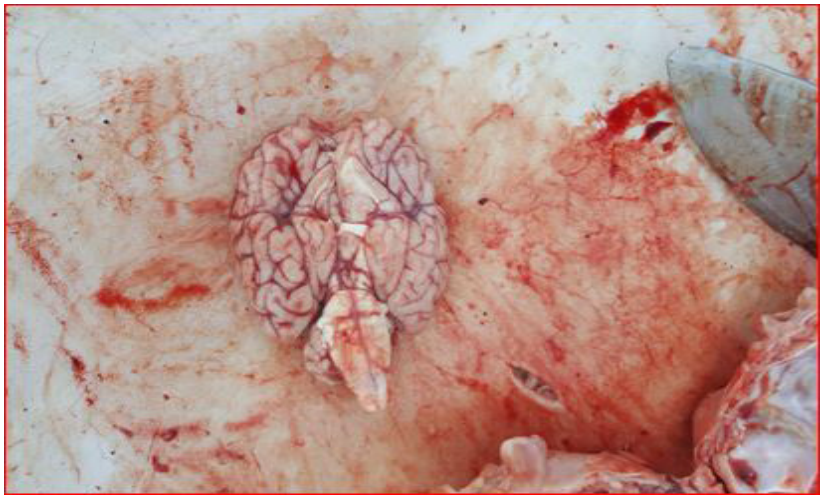

Fig. 3. Severe congestion of the brain of diseased lamb.

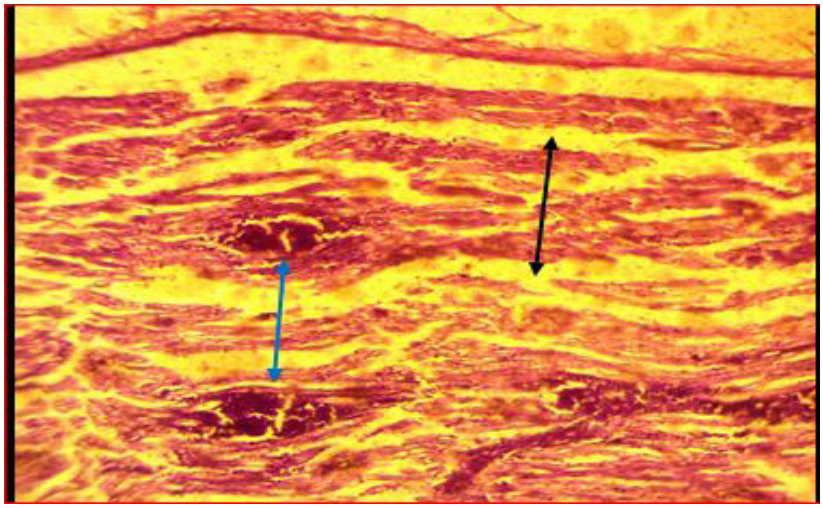

Fig. 4. Histopathological section in the sciatic nerve of diseased lamb showing severe congestion of blood vessels (blue) , with marked edematous fluid in the neural interstia (black). H&E stain. 10X.

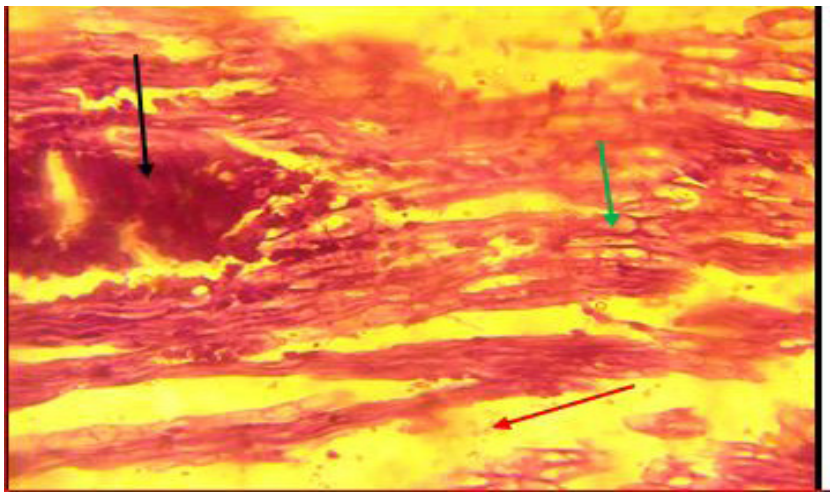

Fig. 5. Histopathological section in the sciatic nerve of sheep showing severe congestion of blood vessels (black), also there is 'marked edematous fluid in the neural interstia (redThere is also an obvious area of vacuolated neural cells (green). H&E stain. 40X.

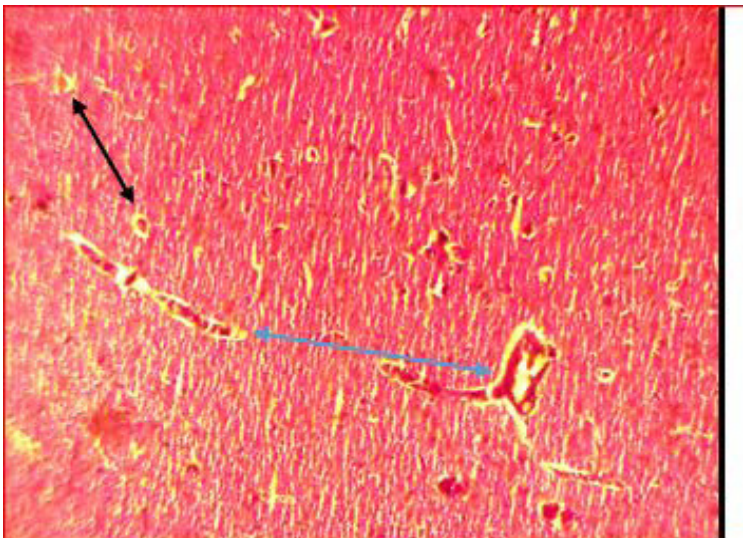

Fig. 6. Histopathological section in brain of diseased lamb, showing severe perivascular edema (black), in addition to perineural edema (blue). H&E stain. 10X.

Discussion

Copper is a mineral of importance to form and function of the CNS [13]. Following the absorption of his mineral from the animal's elementary canal, it is distributed to all the body organs and tissues of the animal through the blood, since blood is copper is distributed to the body only through the blood [1]. Copper ion metabolism has been studiedin animals as well as in humans by different specifically designed models [2].

The complex nature of copper metabolism is shown in the way of its functions as a prosthetic group in different metalloenzymes and is also, in fact, as a cofactor for at least 30 different enzymes. Copper has an association mostly in ceruloplasmin and albumin and its excretion from the gallbladder in the bile [14].

PCD and SCD result in swayback, SD causes very substantial economic losses to the ruminant farming sector as has been mentioned earlier, affecting up to more than 40-50% of the cattle population in different areas and may be less than 50-60% of the lamb population, particularly in areas with forage grown on copper-depleted land [15].

Copper deficiency (hypocuprosis) blocks the proper functioning of copper metalloenzymes, most of which is considered as an important aspect of antioxidant protection and preservation mechanism which involves ceruloplasmin and copper/zinc superoxide dismutase. Moreover, copper which catalyzes these two enzymes, and leading to the dismutation of super peroxide anion, which in turn has a neutralizing effect on hydrogen peroxide and molecular oxygen. ceruloplasmin facilitates the conversion of the ferrous form of iron to ferric to help with the synthesis of erythrocytes [2].

Diagnosis of copper can be done by signs and symptoms shown by diseased animals and verifying the copper serum and liver levels. Disease status can be divided into copper depletion, copper deficiency, body dysfunction, and disease in copper deficient animals [6].

Diseased lambs exhibit varying clinical signs, which are already mentioned by [1,2,4]. Principal clinical data for individual lamb are documented in Table 1. Since most of the animals were suffering from limb movement problems, they were recumbent for the duration of the study and their limbs were unable to support their body weight. Furthermore, several of them exhibited secondary flexor contracture of the forelimbs and other recumbent animals were observed to show spasmodic contractions of the hind limbs periodically.

It has been suggested that the etiology of the de-myelinating disorder in lambs can be considered from a novel perspective, but there is still much work to be done to identify the precise physiological role of copper in respect of myelin metabolism, Furthermore, no options have been offered so far regarding other demyelination

diseases with the same causal basis, as it is very possible that the issue associated with them are diverse and the demyelination lesion is merely a relatively restricted reaction of the neural system to some factors. This work does, nevertheless, proposes an approach for a thoroughly comprehensive investigation of the system that drives demyelination [7]. On the other hand, it has been clarified that In the hypothesized cause of the demyelinating issues there is still need for much more work much more research to be done as efforts to address the etiology have not succeeded and while different acceptable hypotheses have been proposed, none of them has been shown to have received general consensus [16]. As such, identifying any matching circumstances in animals would be beneficial, as the animals could then be monitored at different stages of the disease and experiments performed [13].

It has been proved that, Enzootic ataxia is the highest manifestation of copper deficiency in lambs up to the age of 30-180 days, more or less, and is typically shown by demyelination of the central neural system and by manifestations of incoordination of the hind limbs and, to a lesser degree, the front legs, resulting in unsteady gait, limp or spastic paralysis, and complete inability to walk and eventual demise. There are two types of enzootic ataxia noted and explained on the basis of the lesion site and the chronology of the condition. The congenital form, which is distinguished by severe damage to the cerebral white matter and affects neonates in their early life and the late form which is manifested as tears or cuts to the brain stem and spinal cord motor tracts, with prevalence mostly following week three of life [17].

Chemical analyses indicated that the copper content of blood and liver from the present cases was significantly lower compared healthy lambs of the same age and might also be lower than the copper content of their dams .On the other hand, the blood copper of the diseased lambs and their mothers appeared to be related. Meanwhile, there was a confusion regarding the blood copper of ewes in a specific area, which was significantly below that of ewes from a control area and in a number of cases was similarly low as in ewes which bore swayback diseased lambs [18].

Biochemical analysis of diseased lambs shows significant increase of ALT,AST and CPK, and similar results were also documented by [19]. Elevation of specific enzymes indicated muscle damage and necrosis, which are indicated in the current study .

Gross and histopathological changes of diseased lambs show different changes which agree with [1,2,20], whom mentioned that slightly affected lambs exhibit only microscopic pathological variances comprising neuronal tears or cuts in the red nucleus and demyelination in the spinal cord motor tract. Other serious cases demonstrate, additionally, gross symmetrical cerebral demyelination of different severity.

Histologically, demyelination is described as "the constant and probably the primary lesion, the most severe type being represented by an almost total loss of cerebral myelin, affecting all zones in a diffused manner." In several instances, all phases are observed , and range from the severe type to small symmetrical foci of demyelination frequently found, for instance, in cases without manifestations of any gross alterations. Where liquefaction was widespread the white matter was confined to just a thin sub-cortical layer which formed a margin to a cavity. The demyelination process appeared to take place particularly rapidly, as collections of stainable lipoid, even though often perceived were never absent in gross amounts. Inflammatory cell infiltration and inclusion bodies are not present [13,16,17]. Moreover, [2,7]. added, that the mean histopathology features involve cerebellar tears or cuts and loss of the Bergmann glial cells. These alterations were observed as patches of degeneration loss of the Purkinje both in the vermis and in the hemispheres. Damaged Pur-cells and reactive prolifkinje cells exhibited vacuolation, chromatolysis, and hyalinization of their cytoplas. Furthermore, the same type of tears or cuts was noted in some neurons of the vestibular nucleus and reticular formation of the medulla oblongata. These tears and cuts comprised deficiency of stainable myelin, degenerated and lost myelinated axons, and absence of inflammatory cells [21]. It has been considered that, the major cause of the majority of neural lesions is the malfunctioning of enzymes that depend on copper, particularly superoxide dismutase, which plays a major role in the body's antioxidant protection system [22]. On the other hand, it has also been documented that, The unusual alterations in the cerebral cortex of SD animal encompass cavitation and vacuolation, some glioma, damaged cortical

neurons, and vacuolation of perivenous and perineuronal areas. However, when cells die, the re-absorption creates empty spaces which result in vacuolation and cavitation, and because of this, this brain of a SD animal provides a spongy appearance [7,20]. Kumar (2006) [23], also added that cortical neurons are severely damaged. However, sometimes a new feature called "astrogliosis" in swayback and degenerative alterations may also be noticed in the brain parenchyma, which might be caused by oxygen deficiency because of cerebral edema .

Conclusions

It was concluded that, Swayback disease of young lambs has clear adverse effects which can be minimized by managing the maternal copper status to increase its secretion in the milk.

Ethical considerations

All universally agreed upon ethical methods were used to deal with the study animals

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Competing interest statement

In the current study , The authors certify and acknowledge there is no Competing interest statement.

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مرض التمايل الخلفي في حملان محافظة البصرة ، العراق

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شُخص مرض التمايل الخلفي في حملان محافظة البصرة ، العراق . إذ اظهر ست وأربعون من الحملان المحلية بعمر (اسبوع – ثلاثة اشهر) ومن كلا الجنسين علامات سريرية منها التمايل والترنح ، كما استخدم عشرة من الحملان المحلية السوية سريرياً كمجموعة سيطرة ، اذ خضعت جميع حيوانات الدراسة الى فحوصات سريرية كاملة . اظهرت الحملان المريضة علامات سريرية تمثلت بالترنح والتمايل الخلفي للساقيين ، عدم القدرة على الرضاعة من الامهات ، فقدان وزن الجسم واللامبالاة ، صعوبة في الوقوف بعد ألاستلقاء ,السقوط المتكرر على الارض مع فترات استلقاء طويلة . اظهرت نتائج الفحوصات الدموية وجود فقر الدم من النوع ذي الكريات سوية الحجم والصباغ مع عدم وجود أي تغيرات في العدد الكلي او التفريقي لخلايا الدم البيض . فضلا عن ذلك فقد اظهرت نتائج الدراسة تناقص معنوي في معدلات النحاس في الحملان المريضة بالمقارنة مع حملان مجموعة السيطرة كما سجل ارتفاع معنوي في خمائر الالنين ناقلة الامين والاسبارتيت ناقلة الامين والفوسفاتاز القاعدية في الحملان المريضة بالمقارنة مع حملان مجموعة السيطرة .

أشارت التغيرات النسجية للعصب الوركي للحملان المريضة إلى وجود سائل و ذمي ملحوظ في الفاصل العصبي البطيء ، بالإضافة إلى منطقة ملحوظة من الخلايا العصبية المتخلفة مع احتقان حاد للأوعية الدموية ، ومنطقة واضحة من الخلايا العصبية المفرغة ومن ناحية أخرى ، تم الكشف عن وذمة محيطية شديدة بالإضافة إلى وذمة حول الشرج في الدماغ ، استنتج من هذه الدراسة ان مرض التمايل الخلفي في الحملان له اثار ضارة سلبية للحملان المصابة والتي يمكن التغلب عليها بتنظيم معدلات النحاس لدى الامهات الحلوبة المرضعة .