Hypothyroidism was induced in dogs by three methods. The first method was drug-induced hypothyroidism by Sulphamethoxazole-Trimethoprim combination. The second method was thyroidec- tomy-induced hypothyroidism (surgical removal of thyroid gland), and the third method was ligation-induced hypothyroidism (surgical ligation of thyroid arterial blood supply). The most common clinical signs appeared in three groups after induction were lethargy, weight gain, alopecia, and other dermatological changes. The biochemical changes included hypercholesterolemia, hypertriglyceridemia, elevated liver enzymes (AST, ALT), hypocalcaemia, hypophosphatemia, hypernatremia. Ultrasonographic changes of thyroid gland in drug-induced hypothyroidism showed increase in both total and relative thyroid volume with decreased relative echogenicity. In ligation-induced hypothyroidism the total and relative thyroid volume and also the relative echogenicity were decreased. Histo-pathological changes of thyroid gland revealed hyperplasia of glandular epithelium with papillary projection into the lumen and lymphocytic cellular infiltration, and desquamation of lining epithelium in drug-induced hypothyroidism. In ligation-induced hypothyroidism, thyroid follicles were atrophied with hypertrophy of lining epithelium.

KEY WORDS: Hypothyroidism, Ligation, Thyroidectomy, Thyroxine, Ultrasound

1. INTRODUCTION

Hypothyroidism is the most common endocrinopathy of dog occurs due to impaired production and secretion of the thyroid hormones, which results in a decreased metabolic rate [1, 13]. Hypothyroidism may occur owing to dysfunction of any part of the hypothalamic-pituitary-thyroid axis. Most cases of acquired canine hypothyroidism are caused by primary hypothyroidism due to lymphocytic thyroiditis or idiopathic thyroid atrophy [10]. Primary hypothyroidism is the commonest disorder in dogs results from problems within the thyroid gland, usually destruction of thyroid gland. The two most common causes of this disorder are lymphocytic thyroiditis, and idiopathic atrophy of thyroid gland. There are other causes of primary hypothyroidism such as neoplastic destruction, and iatrogenic causes as; surgical removal of thyroid gland, antithyroid medication, radioactive iodine treatment, and drugs as sulfamethoxazole [14, 21, 35]. Secondary hypothyroidism is a pituitary dependent hypothyroidism which resulted from the insufficient secretion of TSH by the pituitary gland [10, 19, 26, 38]. Tertiary hypothyroidism is theoretically caused by decreased hypothalamic thyrotropin releasing hormone secretion and less common in dogs [21, 28, 32]. Congenital hypothyroidism is rare and most often...
results in early postnatal death [15, 24]. The main problem in the overdiagnosis of hypothyroidism is that all current thyroid tests are affected by other diseases and lowered by many drugs. This has been referred to as the sick euthyroid syndrome has been best documented in very sick dogs [7, 33, 37]. Clinical signs of hypothyroidism, including weight gain, thin hair coat, alopecia, seborrhea, weakness, and lethargy were present in all hypothyroid dogs [23]. Haematological changes such as mild normocytic, normochromic, nonregenerative anaemia and serum biochemical abnormalities such as hypercholesterolemia, hyperlipidemia and hypertriglycerideraemia can indicate hypothyroidism [29]. Hypothyroidism is usually associated with biochemical changes [25]. Tests currently available for diagnosing thyroid disease include; total thyroxine (TT4), total triiodothyronine (TT3), free T4 (fT4), endogenous canine thyroid stimulating hormone (cTSH), TSH response test [16, 18]. Ultrasonography of the thyroid gland also has been used as a diagnostic aid in the diagnosis of primary hypothyroidism [27, 36, 40]. Histologically there is multifocal or diffuse infiltration of the thyroid gland by lymphocytes, plasma cells, and macrophage, the remaining follicles are small, and lymphocytes, macrophages, and degenerate follicular cells may be found within vaculated colloid [1, 10, 17, 33]. This work aim to investigate the clinical picture and determine the biochemical, histopathological and ultrasonographic changes occurring in dogs with experimentally-induced hypothyroidism

2. MATERIAL AND METHODS

The present study was carried out on twenty five apparently healthy stray dogs of an age 2-4 years and body weight 11-23 kg, during the period between February and October 2011. All dogs were dewarmed with systemic anthelmentic (Ivomac super®, 1ml/50kg Bwt.), and were left for 15 days for acclimatization before the beginning of the experiment. The dogs were divided randomly into two groups as following:

Group I: included two subgroups:

Subgroup A: (n=5) were given sulphanmethoxazole- trimethoprine (Septazole® suspention) within a highly dose of 7.5 ml / 10 kg. body weight (~ 30 mg/kg. B.w. of sulphanmethoxazole) orally, 12 hrs. apart for six weeks [39].

Subgroup B: (n=5) were subjected to the experiment and supplemented with normal saline all the period of experiment as a control group from the drug induced hypothyroidism.

Group II: included three subgroups as the following:

Subgroup A: (n=5) were subjected to experimental induction of hypothyroidism by surgical removal of thyroid gland [12].

Subgroup B: (n=5) were subjected to experimental induction of hypothyroidism by surgical ligation of the arterial blood supply of the thyroid gland.

Subgroup C: (n=5) were used as a control for the surgical induction of hypothyroidism (sham-operated dogs). The dogs of all groups were subjected to clinical, biochemical, ultrasonographic, and histo-pathological examination weekly until the end of the experiment.

3. RESULTS

3.1. The clinical signs:

The common clinical signs appeared on the three groups of the induced hypothyroidism were lethargy, weight gain, and dermatological changes in the form of alopecia, poor hair growth, and nodules like form in the skin.

3.2. The biochemical analysis:

The biochemical analysis of drug-induced hypothyroidism showed significant
Experimentally-induced hypothyroidism in dogs.

(p≤0.05) decrease in TT3 and TT4 with significant (p≤0.05) increase in TSH (Table 1). There was a significant (p≤0.05) increase in glucose, total cholesterol, and also triglycerides (Table 1). Elevated liver enzyme (AST, ALT), and significant (p≤0.05) increase in urea and creatinine kinase (Table 1). Serum electrolyte showed significant (p≤0.05) decrease in calcium and sodium levels while there was a significant (p≤0.05) increase in phosphorus, chloride, and non-significant increase in potassium compared with its control group (Table 1). The biochemical analysis of thyroidectomy-induced hypothyroid dogs showed gradual significant (p≤0.05) decrease in TT3, and TT4 with gradual increase in TSH (Table 3). There was a significant (p≤0.05) decrease in glucose level, and significant (p≤0.05) increase in total cholesterol, and triglycerides (Table 3). Elevated liver enzymes (AST, ALT), and significant (p≤0.05) increase in urea level while gradually non-significant increase in creatinine kinase (Table 3). Serum electrolytes showed significant (p≤0.05) decrease in calcium and sodium levels while there was a significant (p≤0.05) increase in phosphorus, chloride, and potassium compared with its control sham-operated group (Table 3). The biochemical analysis of ligation-induced hypothyroidism showed significant (p≤0.05) decrease in both TT3, and TT4 while significantly (p≤0.05) increased TSH (Table 3). There was a significant (p≤0.05) decrease in glucose level, and significant (p≤0.05) increase in total cholesterol, and triglycerides (Table 3). Elevated liver enzymes (AST, ALT), while there was no significant changes in urea level with significant (p≤0.05) decrease of creatinine level (Table 3). Electrolytes showed a significant (p≤0.05) decrease in calcium and significant increase in phosphorus, potassium and chloride while there was non-significant decrease in sodium level compared with its control sham-operated group (Table 3).

3. Ultrasonographic examination:

US of thyroid gland of drug induced hypothyroidism showed significant (p≤0.05) increase in both thyroid volume and relative thyroid volume while significant (p≤0.05) decrease in relative echogenicity compared with control group (Table 2, Figures 1-4).

US of thyroid gland of ligation-induced hypothyroidism showed significant (p≤0.05) decrease in thyroid volume and relative thyroid volume and also relative echogenicity (Table 2, Fig. 5-8).

3.4. The histopathological examination:

Normal microscopic appearance of the thyroid gland of control group (Fig. 9, 10). The histo-pathological changes of drug-induced hypothyroidism showed hyperplasia of glandular epithelium with papillary projection into the lumen and lymphocytic cellular infiltration. Some syncytial epithelial cells with desquamation of lining epithelium and necrotic cellular debris were seen in the lumens of some glands. Thyroid gland of ligation-induced hypothyroidism showed some thyroid follicles showed cystic dilatation with retained secretion in their lumen and flattened lining epithelium, and the adjacent thyroid follicles were atrophied with hypertrophied lining epithelium compared with no microscopic changes in sham-operated group (Fig. 11, 12).

4. DISCUSSION

The clinical signs appeared on the three groups of the induced hypothyroidism were lethargy, weight gain, and dermatological changes included alopecia, poor hair growth, and nodules like form in skin [4, 23, 24].
Yousif et al. (2012)

### Table 1 Changes in thyroid hormones, metabolites and electrolytes in drug-induced hypothyroidism compared with control.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>2nd week</th>
<th>3rd week</th>
<th>4th week</th>
<th>5th week</th>
<th>6th week</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Drug-induced</td>
<td>Control</td>
<td>Drug-induced</td>
<td>Control</td>
</tr>
<tr>
<td>TT3</td>
<td>1.67±0.16</td>
<td>0.98±0.05**</td>
<td>1.63±0.17</td>
<td>1.02±0.06*</td>
<td>1.47±0.17</td>
</tr>
<tr>
<td>TT4</td>
<td>10.72±0.58</td>
<td>11±0.68</td>
<td>10.82±0.78</td>
<td>9.39±0.49</td>
<td>10.02±0.66</td>
</tr>
<tr>
<td>TSH</td>
<td>2.61±0.2</td>
<td>5.95±1.04*</td>
<td>3.02±0.11</td>
<td>5.8±1*</td>
<td>3.24±0.08</td>
</tr>
<tr>
<td>Glucose</td>
<td>81±1.33</td>
<td>103±8*</td>
<td>76.7±1.1</td>
<td>96±6*</td>
<td>82.3±1.6</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>204±7.33</td>
<td>342±11.3**</td>
<td>213±6</td>
<td>383.3±10.4**</td>
<td>209.3±4.9</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>62±2</td>
<td>115±16*</td>
<td>66.7±1.8</td>
<td>132.7±26.2*</td>
<td>65±1.33</td>
</tr>
<tr>
<td>AST</td>
<td>31±1.33</td>
<td>34.7±1.1</td>
<td>34.3±1.8</td>
<td>39.3±1.1*</td>
<td>33±1.33</td>
</tr>
<tr>
<td>ALT</td>
<td>26.7±3.78</td>
<td>66.7±6.4*</td>
<td>34.3±4.22</td>
<td>82.3±14.2*</td>
<td>31±2.67</td>
</tr>
<tr>
<td>Urea</td>
<td>30.7±1.1</td>
<td>42±0.67**</td>
<td>32±0.67</td>
<td>40±0.67**</td>
<td>33.3±0.89</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.68±0.02</td>
<td>0.92±0.03**</td>
<td>0.71±0.03</td>
<td>0.94±0.11</td>
<td>0.76±0.03</td>
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<tr>
<td>Calcium</td>
<td>8.98±0.9</td>
<td>9.72±0.54</td>
<td>8.77±0.11</td>
<td>9.12±0.72</td>
<td>8.9±1.04</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>3.35±0.3</td>
<td>4.12±0.18*</td>
<td>3.71±0.16</td>
<td>4±0.14</td>
<td>3.62±0.19</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.27±0.33</td>
<td>4.31±0.06</td>
<td>4.39±0.32</td>
<td>4.16±0.05</td>
<td>4.2±0.3</td>
</tr>
<tr>
<td>Sodium</td>
<td>142.7±2.9</td>
<td>149.7±1.1*</td>
<td>128.7±2.4</td>
<td>154.7±1.1**</td>
<td>142.7±4.4</td>
</tr>
<tr>
<td>Chloride</td>
<td>87.3±7.1</td>
<td>121.3±2.4*</td>
<td>83.7±4.9</td>
<td>132.3±7.6*</td>
<td>88±4.7</td>
</tr>
</tbody>
</table>

Data are presented as mean (±S.E.). * Means significantly different from control at P<0.05. ** Means highly significantly different from control at P<0.001

### Table 2 Ultrasonographic changes of thyroid gland in drug-induced hypothyroidism compared with control.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2nd week</th>
<th>3rd week</th>
<th>4th week</th>
<th>5th week</th>
<th>6th week</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Drug-induced</td>
<td>Control</td>
<td>Drug-induced</td>
<td>Control</td>
</tr>
<tr>
<td>Total volume (ml)</td>
<td>2.04±0.24</td>
<td>2.52±0.21</td>
<td>2.12±0.17</td>
<td>3.2±0.45*</td>
<td>2.39±0.42</td>
</tr>
<tr>
<td>Relative vol. (ml/ kg&lt;sup&gt;3/75&lt;/sup&gt;)</td>
<td>0.27±0.02</td>
<td>0.35±0.02*</td>
<td>0.28±0.02</td>
<td>0.43±0.03*</td>
<td>0.31±0.06</td>
</tr>
<tr>
<td>Relative echog. (%)</td>
<td>1.11±0.45</td>
<td>0.68±0.02*</td>
<td>1.08±0.15</td>
<td>0.49±0.04*</td>
<td>0.99±0.25</td>
</tr>
</tbody>
</table>

Data are presented as mean (±S.E.). * Means significantly different from control at P<0.05. ** Means highly significantly different from control at P<0.001.
Experimentally-induced hypothyroidism in dogs.

Table 3 Changes in thyroid hormones, metabolites and electrolytes in drug-induced hypothyroidism compared with sham-operated group

<table>
<thead>
<tr>
<th>Parameters (µg/dl)</th>
<th>Sham.</th>
<th>TIH</th>
<th>LIH</th>
<th>Sham.</th>
<th>TIH</th>
<th>LIH</th>
<th>Sham.</th>
<th>TIH</th>
<th>LIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT3</td>
<td>1.59±0.08</td>
<td>0.69±0.12</td>
<td>1.38±0.05</td>
<td>0.41±0.08**</td>
<td>0.7±0.08**</td>
<td>1.05±0.04</td>
<td>0.42±0.06**</td>
<td>0.37±0.03**</td>
<td>1.76±0.03</td>
</tr>
<tr>
<td>TT4</td>
<td>9.77±0.36</td>
<td>8.16±0.44*</td>
<td>8.68±0.68</td>
<td>8.47±0.36</td>
<td>5.59±0.56</td>
<td>6.07±1.1</td>
<td>8.18±0.38</td>
<td>5.83±0.56</td>
<td>3.68±0.45**</td>
</tr>
<tr>
<td>TSH</td>
<td>4.06±0.64</td>
<td>5.48±0.49</td>
<td>5.57±0.93</td>
<td>3.47±0.64</td>
<td>12.1±0.55**</td>
<td>6.55±1.43</td>
<td>3.29±0.65</td>
<td>37.1±1.78**</td>
<td>18.5±0.36**</td>
</tr>
<tr>
<td>Glucose</td>
<td>100±6.7</td>
<td>90±8</td>
<td>109±9.3</td>
<td>105.3±6.4</td>
<td>71.7±6.4</td>
<td>110±8</td>
<td>110.3±6.4</td>
<td>67.6±6.7</td>
<td>102±8</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>209.7±19.6</td>
<td>205±4.7</td>
<td>216.7±10.4</td>
<td>217.7±17.1</td>
<td>193.3±3.6</td>
<td>216.3±15.78</td>
<td>228.7±14.9</td>
<td>221.7±2.2</td>
<td>233.3±18.4</td>
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<tr>
<td>Triglyceride</td>
<td>94.3±6.4</td>
<td>109.3±2.9*</td>
<td>83.7±4.2</td>
<td>96±1.3</td>
<td>121±4*</td>
<td>78±2**</td>
<td>88.7±11.8</td>
<td>137.7±8.4</td>
<td>84.7±1.8</td>
</tr>
<tr>
<td>AST</td>
<td>51.3±1.1</td>
<td>66±6*</td>
<td>98.7±2.4**</td>
<td>49±0.67</td>
<td>70±2.7**</td>
<td>83±4**</td>
<td>42.3±0.44</td>
<td>76.7±3.1**</td>
<td>84.7±3.8**</td>
</tr>
<tr>
<td>ALT</td>
<td>68±3.3</td>
<td>83±4.67</td>
<td>99±12.7*</td>
<td>79.3±1.8</td>
<td>85.3±4.2</td>
<td>95.3±9.6</td>
<td>82.67±2.89</td>
<td>88.3±4.9</td>
<td>91.7±4.9</td>
</tr>
<tr>
<td>Urea</td>
<td>39.7±1.1</td>
<td>43±0.67*</td>
<td>37.7±2.2</td>
<td>42.7±1.8</td>
<td>49.3±1.1*</td>
<td>38.7±2.2</td>
<td>50±0.67</td>
<td>51.3±1.1</td>
<td>42±4</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.97±0.06</td>
<td>0.7±0.05*</td>
<td>0.81±0.08</td>
<td>1.1±0.03</td>
<td>0.88±0.05*</td>
<td>0.82±0.05*</td>
<td>1.21±0.04</td>
<td>1.16±0.05</td>
<td>0.82±0.04*</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.88±0.09</td>
<td>10.07±0.24*</td>
<td>8.46±0.99</td>
<td>8.18±0.13</td>
<td>4.67±0.5**</td>
<td>6.89±0.78</td>
<td>8.43±0.19</td>
<td>4.69±0.38**</td>
<td>4.12±0.17**</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>3.26±0.04</td>
<td>4.02±0.16*</td>
<td>4.6±0.13**</td>
<td>3.27±0.06</td>
<td>7.6±0.6**</td>
<td>3.35±0.51</td>
<td>3.09±0.02</td>
<td>7.34±0.6**</td>
<td>7.17±0.5**</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.37±0.25</td>
<td>3.68±0.11</td>
<td>4.26±0.38</td>
<td>4.53±0.25</td>
<td>5.02±0.09</td>
<td>4.57±0.33</td>
<td>4.04±0.13</td>
<td>5.72±0.07**</td>
<td>4.9±0.25</td>
</tr>
<tr>
<td>Sodium</td>
<td>152±4</td>
<td>152±3.33</td>
<td>144.3±4.2</td>
<td>158.7±3.6</td>
<td>157.3±3.3</td>
<td>137.1±3.1</td>
<td>154±3.3</td>
<td>137.7±3.1</td>
<td>149±1.3</td>
</tr>
<tr>
<td>Chloride</td>
<td>83.7±2.2</td>
<td>98.7±2.9*</td>
<td>110.3±3.8</td>
<td>88.7±1.6</td>
<td>106±3.3*</td>
<td>128±2**</td>
<td>80.7±1.1</td>
<td>98±0.7**</td>
<td>139.3±2.9**</td>
</tr>
</tbody>
</table>

Data are presented as mean (±S.E.). * Means significantly different from control at P≤0.05. ** Means highly significantly different from control at P≤0.001. TIH: thyroidectomy-induced hypothyroidism, LIH: ligation-induced hypothyroidism.

Table 4 Ultrasonography of thyroid gland of ligation groups compared with sham-operated group.

<table>
<thead>
<tr>
<th>Parameters (µg/dl)</th>
<th>Sham.</th>
<th>Ligation</th>
<th>Sham.</th>
<th>Ligation</th>
<th>Sham.</th>
<th>Ligation</th>
<th>Sham.</th>
<th>Ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT3</td>
<td>2.66±0.23</td>
<td>1.21±0.26*</td>
<td>2.82±0.08</td>
<td>0.94±0.22**</td>
<td>2.14±0.08</td>
<td>0.75±0.14**</td>
<td>2.51±0.1</td>
<td>0.62±0.13**</td>
</tr>
<tr>
<td>Relative vol. (µl/kg&lt;sup&gt;0.75&lt;/sup&gt;)</td>
<td>0.3±0.02</td>
<td>0.14±0.04*</td>
<td>0.31±0.01</td>
<td>0.11±0.03*</td>
<td>0.23±0.004</td>
<td>0.08±0.02**</td>
<td>0.27±0.004</td>
<td>0.07±0.02**</td>
</tr>
<tr>
<td>Relative echog. (%)</td>
<td>0.8±0.27</td>
<td>0.49±0.02</td>
<td>0.69±0.08</td>
<td>0.35±0.01*</td>
<td>0.94±0.11</td>
<td>0.34±0.02*</td>
<td>0.79±0.02</td>
<td>0.18±0.05**</td>
</tr>
</tbody>
</table>

Data are presented as mean (±S.E.). * Means significantly different from control at P≤0.05. ** Means highly significantly different from control at P≤0.001. TIH: thyroidectomy-induced hypothyroidism, LIH: ligation-induced hypothyroidism.
Figure 1 Ultrasonographic (US) image of thyroid gland in control group showing hyperechoic compared to sternothyroid muscle in longitudinal section. Figure 2 US of thyroid gland in control group showing oval shape in transverse section (TS). Figure 3 US of thyroid gland in drug-induced hypothyroid dog (6th week) showing hypoechoic and increase volume in longitudinal section (LG). Figure 4 US of thyroid gland in drug-induced hypothyroid dog (6th week) showing oval shape and increase volume in TS. Figure 5 US of thyroid gland of sham-operated dog showing isoechoic compared with sternothyroid muscle in LG. Figure 6 US of thyroid gland of sham-operated dog showing oval shape in transverse section (TS). Figure 7 US of thyroid gland of ligation-induced hypothyroid dog (4th week) showing decreased volume and hypoechogenicity compared with sternothyroid muscle in LG. Figure 8 US of thyroid gland of ligation-induced hypothyroid dog (4th week) showing oval in shape and decreased volume in TS.
Experimentally-induced hypothyroidism in dogs.

The significant decrease in TT3 and TT4 with significant increase in TSH in the three groups of induction indicates the successful induction of hypothyroidism in dogs by any of the three methods (drug induced, thyroidectomy and ligation of thyroid arterial blood supply). The significant increase in glucose level in drug-induced hypothyroidism by potentiated sulfonamide drugs was consistent with other studies (2). The significant increase of cholesterol and triglycerides in the three groups of induction may be attributed to decrease of thyroid hormones that lead to decrease synthesis and degradation of cholesterol as a result increase cholesterol level in the serum [9, 11, 21, 24, 25]. Elevated liver enzymes (AST, ALT) could be the impairment of the liver function which associated with hypothyroidism [20, 22, 31, 34]. Electrolyte analysis showed significant decrease in calcium and significant increase in phosphorus may be attributed to impairment of calcitonin production from thyroid hormone [5], and metabolic derangements induced by thyroid hormone deficiency, such as altered calcium homeostasis (30). The significant decrease in sodium with significant increase in potassium and chloride could be attributed to reduction of GFR secondary to hypothyroidism that leads to increase the excretion of sodium resulting in decrease serum sodium level and elevation of chloride level and potassium level [8]. Hypothyroidism showed significant increase in total

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Figure 9 Normal microscopic appearance of thyroid gland of the control group.

Figure 10 Microscopic appearance of drug-induced hypothyroidism in dogs. Note the presence of hyperplasia of glandular epithelium with papillary projection into the lumen and lymphocytic cellular infiltration. Some syncytial epithelial cells are found in some glands (arrow).

Figure 11 Normal microscopic appearance of thyroid gland of sham-operated dogs.

Figure 12 Microscopic appearance of thyroid gland of ligation group. Note the presence of cystic dilatation in some thyroid follicles with retained secretion in their lumen and flattened lining epithelium. The adjacent thyroid follicles were atrophied with hypertrophied lining.
volume and relative volume that may be attributed to the effect of sulphonamides that have agiotrogenic effect on thyroid gland leading to increase thyroid volume [6]. The decreased relative echogenicity might be due to decreased thyroid gland production of thyroid hormones [3, 27, 36]. On the other hand, significantly decrease in total volume, relative volume and relative echogenicity may be attributed to the ligation of arterial blood supply leading to thyroid gland ischemia leading to decrease volume and homogenous parenchyma [3, 27, 36]. Histopathology showed Hyperplasia of glandular epithelium with papillary projection into the lumen and lymphocytic cellular infiltration. Some syncytial epithelial cells are found in some glands with desquamation of lining epithelium and necrotic cellular debris in microscopic examination of thyroid gland of drug-induced hypothyroid dog [1, 10, 17, 31, 33]. Some thyroid follicles showed cystic dilatation with retained secretion in their lumen and flattened lining epithelium, and the adjacent thyroid follicles were atrophied with hypertrophied lining epithelium in microscopic examination of thyroid gland of ligation group [13].

CONCLUSION

Based upon the results of this work, it can conclude that hypothyroidism was successfully induced under experimental conditions in dogs by administrating Sulphamethoxazole-Trimethoprim combination drug at dose of 30 mg/kg. B.w., PO, Twice daily for six weeks. Hypothyroidism was successfully induced under experimental condition in dogs by surgical removal of thyroid gland (thyroidectomy), and by surgical ligation of thyroid arterial blood supply. Hypothyroidism by all methods produces clinical, biochemical, ultrasonographic, and histo-pathological changes when compared with the control groups. The major clinical findings in the three induced hypothyroidism groups include weight gain, lethargy, dermatological abnormalities as nodular formation and alopecia, poor hair growth, roughness and hyperpigmentation of hair. The major biochemical changes in all types of induced hypothyroidism are hypercholesterolemia, elevated liver enzymes (AST and ALT), and hypertriglyceridemia, and hypocalcemia, hyperphosphatemia, mild hyperkalemia, mild hypercholeremia and hyponateremia. The common ultrasonographic changes in the drug-induced hypothyroidism is characterized by increased total thyroid volume and relative thyroid volume and decreased in relative thyroid echogenicity, while in ligation-induced hypothyroidism is characterized by decreased total thyroid volume and relative thyroid volume and relative thyroid echogenicity. The common histopathological changes in thyroid gland include desquamation and hypertrophied of the lining epithelium of the thyroid follicles. These results highlight the significant role of thyroid gland in maintaining the body metabolism equilibrium and the integrity of many biological organs including liver, heart, kidney, and skin. Hypothyroidism causes changes in the biochemical parameters soon after induction. Therefore TT3 and TT4 together with other biochemical changes could be used to monitor the early detection of thyroid dysfunction.

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5. REFERENCES

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Experimentally-induced hypothyroidism in dogs.

Hamadeh Mahmoud Youssef1, Mohamed Mohamad El Rouf2, Hams El Din Mohamed Abd El Aziz Al-Attia2.

1. Center for Agricultural Research - Production Sector, Mosselat.
2. veterinary medicine - Animal Health Department, Faculty of Veterinary Medicine, Benha University.

The experimental withdrawal of thyroid hormones in dogs was done by three methods as follows:

1. The first group: Total withdrawal of the thyroid gland by using the drugs (Sulfamethoxazol - Trimethoprim) for six consecutive weeks.
2. The second group: Total withdrawal of the thyroids by surgical removal.
3. The third group: Total withdrawal of the thyroid gland by linking the blood supply to the thyroid gland surgically.

The clinical signs that appeared after the withdrawal of thyroid hormones in the three mentioned groups were:

1. Fatigue,
2. Increased weight,
3. Enlargement of the thyroid,
4. The appearance of some changes in the thyroid tissue.
5. Increased fatty tissues,
6. Increased enzyme activity (Kalaemia, AST & ALT),
7. Decrease in serum calcium and sodium concentrations and increase in tetravalent phosphorus.

The ultrasonographic changes of the thyroid gland in the withdrawal group were: an increase in both the size and weight of the gland, and a decrease in the gland density.

The histopathological changes of the thyroid gland showed:

1. Hair loss,
2. Increased fatty tissues,
3. Inflammation of lymph nodes,
4. Excessive shedding of the lining epithelial cells.

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