

Sokoto Journal of Medical Laboratory Science 2020; 5(4): 4 - 11

SJMLS - 5(4) - 001

Dysthyroxinaemia Among Sub-fertile Female Clients Attending Nizamiye Hospital, Abuja, Nigeria. Biliaminu, S.A.*¹, AbdulAzeez, I.M.¹, Khan, N.², Bakr, M.R.², Oladosu, W.O.³, Yusuff, J.O.⁴ and Okesina, A.B.¹

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Abstract

Disorders of thyroid function is very common in the population and affects many systems including the reproductive system, hence its causal role in infertility in women cannot be overemphasized. This makes it relevant in the algorithm of reproductive dysfunction. The aim of this study was to determine the pattern and prevalence of dysthyroxinaemia among infertile females visiting Nizamiye Hospital, Abuja, Nigeria. This was a retrospective study of thyroid function test and other parameters of infertile females in a private hospital setup between January 2015 and December 2019. Data were analyzed using Statistical Software for Social Sciences (SPSS Version 21). The 52 infertile females included in this study had mean age of 32.65±5.21 years. The youngest of them was 22 while the oldest was 42 years old. Twenty-two (42.3%) and 30 (57.7%) of them had primary and secondary infertility respectively. Of all the subjects 20 (38.5%) were euthyroid, 21(40.4%) had 2° hypothyroidism, 9(17.3%) had 1° hypothyroidism while 2(3.8%) had subclinical hypothyroidism. Other variants of dysthyroxinaemia were not present amongst the subjects. There was a higher prevalence of dysthyroxinaemia in our study than in previous studies. However, 2° hypothyroidism was found to be the commonest among the subjects in this study which was essentially in contrast with subclinical hypothyroidism found in previous studies. Thyroid function test should be encouraged in infertile female subjects for proper and prompt management to improve both natural fertility, spontaneous conception as well as conception rates with assisted reproductive therapy.

Keywords: Prevalence, Dysthyroxinaemia, Subfertile Female subjects, Nizamiye Hospital, Abuja, Nigeria.

Introduction

Infertility is defined as failure to achieve pregnancy after at least one year of regular unprotected sexual intercourse in a couple of reproductive age (Vayena *et al.*, 2001). Epidemiological data suggest that infertility affects 10-15% of couples at reproductive age (Unuane *et al.*, 2011; Vayena *et al.*, 2001).

Infertility despite regular unprotected sexual intercourse without any previous pregnancy is defined as primary infertility, whereas fertility problems following a previous experience of pregnancy is defined as secondary infertility (Unuane *et al.*, 2011). Female infertility occurs in about 37% of all infertile couples and ovulatory disorders account for more than half of these.

Wealth is sometimes measured by the number of children a woman has, as well as inheritance of property (Dyer 2012; Araoye, 2003). Children can influence financial security in many ways. In Nigeria and Cameroon, land claims are decided by the number of children. Also, in some sub-Saharan countries a woman may be denied inheritance if she did not bear any child (Dyer, 2012). In some African and Asian countries, a husband can deprive his infertile wife of food, shelter and other basic necessities like clothing (Dyer ,2012; Araoye, 2003). In Cameroon, a woman may lose access to land from her husband and left on her own in old age (Araoye, 2003).

Endocrine system is the second key regulator of organ system function after nervous system. Hormones are the messengers in endocrine signaling. Thyroid gland controls brain and somatic development in infants and metabolic activities in adults. Upon stimulation, the thyroid gland secretes thyroid hormones; triiodothyronine (T3) and thyroxine (T4). Thyroid hormones have a role in controlling basal metabolic rate, growth as well as the development and differentiation of many cells in the body (Habbu and Shaikh, 2016).

The ovaries are in continuous interaction with the other endocrine organs. The interplay may account for infertility occurring at different levels and may render the diagnosis of infertility a difficult exercise for the involved physician. Thyroid disorders, both hyperthyroidism and hypothyroidism, can interact with the ovaries, through a direct effect on ovarian function, but autoimmunity may be involved, as well as alterations of the sex hormone binding protein levels.

Dysthyroxinaemia affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances (Verma *et al.*, 2012). Therefore, normal thyroid function is necessary for optimal fertility in order to achieve and sustain a healthy pregnancy (Verma *et al.*, 2012). Thyroid disease has been described as the most common endocrine condition affecting women of reproductive age (Araoye, 2003). Undiagnosed and untreated thyroid disease can be a cause for subfertility as well as infertility (Kameswaramma, 2016; Cho, 2015; Verma *et al.*, 2012; Krassas *et al.*, 2010; Poppe and Glinoer 2003).

Therefore, assessment of thyroid dysfunction has been considered as an important component in the infertility work-up of women (Kameswaramma, 2016; Krassas *et al.*, 2010). Thyroid evaluations have been advocated for infertile women desiring to conceive, particularly those with personal or family history of thyroid disorder, autoimmune disease, ovulatory dysfunction, or miscarriages (Verma *et al.*, 2012). A comprehensive thyroid evaluation

should include serum triiodothyronine (T3), thyroxine (T4), thyroid stimulating hormone (TSH), and thyroid autoimmune testing such as thyroid peroxidase antibodies (TPOAb), thyroglobin antibodies (TgAb), and thyroid stimulating immunoglobulin (TSI) (Krassas *et al.*, 2010).

Studies have been done on dysthyroxinaemia in infertile female patients in public health set ups in Nigeria. However, fewer ones if any has been done in private hospitals. This study was done to determine the pattern and prevalence of dysthroxinaemia among infertile female Nigerians visiting a private hospital Nizamiye Hospital, Abuja, Nigeria.

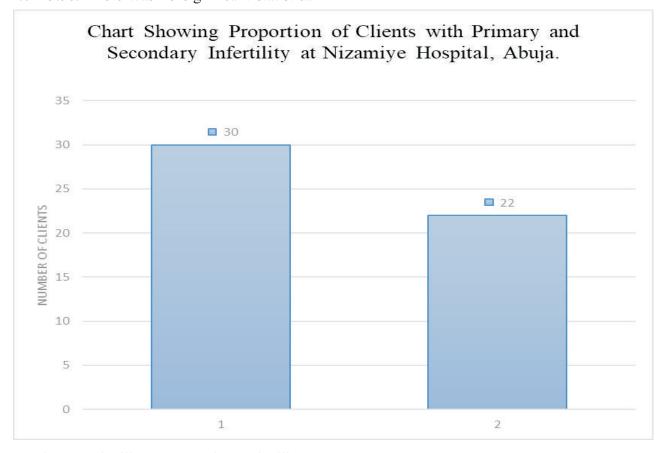
Materials and Method

This was a retrospective study of thyroid function test and other parameters of female partners of infertile couples in a private hospital set up between January 2015 and December 2019. These were used to establish, categorize and determine prevalence of weight disorders among female partners of infertile couples in Nizamiye Hospital, Abuja. Data were analyzed using Statistical Software for Social Sciences (SPSS Version 21).

Results

The mean age (Years)±SD for subjects with primary infertility 32.09±5.44 and secondary infertility 33.07±5.10. The mean ages of the two sub-classes were not statistically different at pvalue of 0.475. Mean duration of marriage (Years)±SD for subjects with primary infertility 4.27±2.00 and secondary infertility 9.87±4.77. The mean ages of the two sub-classes were statistically different (p= 0.000). Mean duration of infertility (Years)±SD for subjects with primary infertility 4.27±2.00 and secondary infertility 5.07±2.79. The mean ages of the two sub-classes were not statistically different (p= 0.242). Table 1 shows the Mean \pm SD age, durations of marriage and infertility in the two classes of infertility. Figure 1 shows the proportion of clients with primary and secondary infertility at Nizamiye Hospital, Abuja. The mean age for the 52 female partners of the infertile couples in this study was 32.65±5.21 years. The youngest of them was 22 while the oldest was 42 years old. Twenty-two (42.3%) of them had primary infertility while 30 (57.7%) of them had secondary infertility. The mean weight, height, BMI and Ponderal Index of the 52 subjects were 82.89±15.45Kg, 1.62±0.07M, 32.07 ± 5.34 Kg/M² and 19.83 ± 3.63 Kg/M³ respectively. Table 2 shows the mean±SD of anthropometric parameters of all infertile female clients attending Nizamiye Hospital, Abuja. The Mean±SD fT3, fT4 and TSH in the two classes of infertility as follows: Mean fT3±SD in pmol/L for subjects with primary infertility 3.61±1.31, and secondary infertility 3.31±1.07. The mean fT3 of the two sub-classes were not statistically different at p-value of 0.809. The Mean±SD fT4 in pmol/L for subjects with primary infertility was 8.59±7.44 while that of secondary infertility was 16.89±5.61. There was significant statistical difference between the two fT4 at p-value of 0.001. The mean TSH±SD in mIU/ml for subjects with primary infertility was 3.30±2.28 while that of secondary infertility was 2.61±3.58. There was no significant statistical

difference between the two TSH at p-value of 0.798. Table 3 shows the Mean±SD of serum fT3, fT4 and TSH in Clients with Primary and Secondary Infertility Attending Nizamiye Hospital, Abuja. A total of 20(38.5%) infertile female subjects were euthyroid. The remaining 32(62.5%) had various categories of dysthyroxinaemia as follows: 1° hypothyroidism 9(17.3%), 2° hypothyroidism 21(40.4%) and subclinical hypothyroidism 2(3.8%). Among the primary infertility clients, 4(7.7%) were euthyroid, six (11.5%) had 1° hypothyroidism while 12(23.1%) had 2° hypothyroidism. Within the secondary infertility clients, 16(30.8%) were euthyroid, while 12(23.1%) had 2° hypothyroidism. In all, none of them had hyperthyroidism of any form be it primary, secondary nor subclinical. Table 4 show the prevalence and frequency of functional Dysthyroxinaemia in clients with Primary and Secondary Infertility attending Nizamiye Hospital, Abuja.



1=Primary Infertility, 2=Secondary Infertility

Figure 1: Chart Showing Proportion of Clients with Primary and Secondary Infertility at Nizamiye Hospital, Abuja



Table 1: Mean±SD Age, Marriage and Infertility Duration Clients with Primary and Secondary Infertility Attending Nizamiye Hospital, Abuja

Parameters	All Sub- fertile Subjects	Primary Infertility Subjects	Secondary Infertility Subjects	p-Values
Age (Years)±SD	32.65±5.22	32.09±5.44	33.07±5.10	0.475
Duration of				
Marriage (Years)	7.50 ± 4.73	4.27 ± 2.00	9.87 ± 4.77	0.000
$\pm SD$				
Duration of				
Infertility (Years)	4.73 ± 2.50	4.27 ± 2.00	5.07 ± 2.79	0.242
$\pm SD$				

Table 2: Mean±SD Anthropometric Parameters of all Infertile Female Clients Attending Nizamiye Hospital, Abuja.

Anthropometric Parameters	Mean±SD		
Age (Years)	32.65±5.21		
Weight (Kg)	82.89 ± 15.45		
Height (M)	1.62 ± 0.07		
BMI (Kg/M^2)	32.07 ± 5.34		
Corpulence Index (Kg/M ³)	19.83±3.63		

Table 3: Mean±SD Serum fT3, fT4 and TSH in Clients with Primary and Secondary Infertility Attending Nizamiye Hospital, Abuja.

Parameters	All Sub-fertile Patients	Primary Infertility Subjects	Secondary Infertility Subjects	p-Values
fT3(pmol/L)±SD	3.44±1.18	3.61±1.31	3.31±1.07	0.809
fT4(pmol/L)±SD	13.38 ± 7.61	8.59 ± 7.44	16.89 ± 5.61	0.001
TSH(mIU/L)±SD	2.90 ± 3.09	3.30 ± 2.28	2.61 ± 3.58	0.798

Table 4: Prevalence and Frequency of Functional Dysthyroxinaemia in Clients with Primary and Secondary Infertility Attending Nizamiye Hospital, Abuja.

Functional	All Sub-fertile	Primary	Secondary
Dysthyroxinaemia	Patients	Infertility	Infertility
		Subjects	Subjects
Euthyroidism	20(38.5%)	4(7.7%)	16(30.8%)
1° Hyperthyroidism	-	-	-
2° Hyperthyroidism	-	-	-
1° Hypothyroidism	9(17.3%)	6(11.5%)	-
2° Hypothyroidism	21(40.4%)	12(23.1%)	12(23.1%)
Subclinical	-	-	-
Hyperthyroidism			
Subclinical	2(3.8%)	-	2(3.8%)
Hypothyroidism			
Sick Euthyroid State	-	-	-
Total	52(100%)	22(42.3%)	30(57.7%)

Discussion

Infertility despite regular unprotected sexual intercourse without any previous pregnancy is defined as primary infertility, whereas fertility problems following a previous experience of pregnancy is defined as secondary infertility (Unuane *et al.*, 2011). Female infertility occurs in about 37% of all infertile couples and ovulatory disorders account for more than half of these. Infertility is defined as failure to achieve pregnancy after at least one year of regular unprotected sexual intercourse of a couple at reproductive age (Unuane *et al.*, 2011). Epidemiological data suggest that infertility affects 10-15% of couples at reproductive age (Unuane *et al.*, 2011; Vayena *et al.*, 2001).

Thyroid disorders, both hyperthyroidism and hypothyroidism, can interact with the ovaries, through a direct effect on ovarian function, but autoimmunity may be involved, as well as alterations of the sex hormone binding protein levels.

Dysthyroxinaemia affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances (Kameswaramma, 2016). Therefore, normal thyroid function is

necessary for optimal fertility in order to achieve and sustain a healthy pregnancy (Kameswaramma, 2016). Thyroid disease has been described as the most common endocrine condition affecting women of reproductive age (Araoye, 2003).

In this study, the mean age for the 52 female partners of the infertile couples in this study was 32.65±5.21 years. The youngest of them was 22 while the oldest was 42 years old. The mean age in years±SD for subjects with primary infertility 32.09±5.44 and secondary infertility 33.07±5.10. The mean ages of the two sub-classes were not statistically different (p=0.475). In a similar study done at Ahmadu Bello University Teaching Hospital, Zaria, Nigeria, the age ranged between 18 and 48 years with mean age of 31.3±6.4 (Aliyu *et al.*, 2017). This shows that there was similarity between age range of occurrence of infertility among infertile female in this study and that in Zaria (Aliyu *et al.*, 2017).

Forty-two percent (42%) of all the clients had primary infertility while 58% had secondary infertility. This observation is in contrast with findings in other studies in which there was predominance of primary infertility over secondary as depicted with the Port-Harcourt study with 62.6% of patients having primary

infertility while 37.4% had secondary infertility (Orazulike and Odum., 2018) and the Indian one with 63.01% versus 36.9% for primary and secondary infertility respectively (Nasir et al., 2016).

In our study 38.5% of the infertile female subjects were euthyroid while the remaining 61.5% had various categories of dysthyroxinaemia as follows: 1° hypothyroidism 17.3%, 2° hypothyroidism 40.4% and subclinical hyperthyroidism 3.8%. In a similar study done in Kano, thyroid disorders were observed in 23.4% of the subjects (Emokpae et al., 2011). The prevalence of thyroid dysfunction in infertile women was found to be 33.3% in a study in India (Rahman et al., 2008). Two studies, also Indian based had prevalence of 23% (Sharman et al., 2012) and 42% (Shivaleela et al., 2012) respectively. Also, in another study, 25.6% of the study populations had thyroid dysfunction which possibly resulted in infertility. Majority of thyroid dysfunction was hypothyroidism comprising 20.1%, out of which subclinical hypothyroidism was the most common was 11.8% (Rijal et al., 2011). All these demonstrated relatively high prevalence. However, a study done in Port Harcourt showed a much lower prevalence (4.6%) of thyroid disorders in infertile women (Orazulike and Odum, 2018). The relatively higher prevalence of dysthyroxinaemia in this study might not be unconnected with the high BMI in these patients.

Prevalence of hypothyroidism, (primary and secondary) in this study was 57.7%. There was no case of subclinical hypothyroidism. This was in sharp contradiction to previous studies done, in which prevalence of hypothyroidism in women with infertility, particularly subclinical hypothyroidism, was more common and has been reported to vary from 0.7% to 43% (Poppe *et al.*, 2007). This wide range of prevalence has been attributed to the differences in sensitivity of serum TSH measurement (Cho 2018; Krassas *et al.*, 2010; Poppe *et al.*, 2008; Poppe and Glinoer 2003). In another study, 0.9% of patients had overt hypothyroidism (Rahman *et al.*, 2008).

Among the female subjects with primary infertility, 7.7% were euthyroid. 11.5% had 1°

hypothyroidism while 23.1% had 2° hypothyroidism in this study. In this study, hypothyroidism (both primary and secondary) was more in subjects with primary infertility. This finding is at variance with another study done in India in which the prevalence of hypothyroidism was more in clients with secondary infertility (Fupare *et al.*, 2015).

Within the secondary infertility subjects, 30.8% were euthyroid, while 23.1% had 2° hypothyroidism. In all the clients, none of them had hyperthyroidism of any form be it primary, secondary nor subclinical.

In our study, the mean±SD fT3, fT4 and TSH in the two classes of infertility as follows: Mean fT3±SD in pmol/L for subjects with primary infertility was 3.61±1.31 while that of secondary infertility was 3.31±1.07. There was no statistically significantly difference in the mean fT3 of the two sub-classes (p=0.809). For fT4, the mean±SD in pmol/L for subjects with primary infertility was 8.59±7.44 while that of secondary infertility was 16.89±5.61. This shows a significant statistical difference between the two for fT4 (p=0.001). In the case of TSH, the mean±SD in mIU/ml for subjects with primary infertility was 3.30±2.28 while that of secondary infertility was 2.61±3.58. There was no significant statistical difference between the two for TSH (p=0.798).

Our findings in this study might not be unconnected with elevated BMI in our clients. Most of the studies done were in tandem with our findings. For example, in a previous study, it was found that BMI positively correlated with serum TSH, negatively to serum free T4 (FT4) and had no correlation to serum free T3 (FT3) (Knudsen et al., 2005). In another study, morbidly obese women (BMI > $40 \square \text{kg/m}^2$) had higher TSH levels than others with moderate obesity (BMI < 40 □ kg/m²), and TSH values were positively correlated to BMI in euthyroid subjects. In addition, lower FT4 values were accompanied by higher BMI values, but no relationship between BMI and FT3 was found (Iacobellis et al., 2005). Another study showed that morbidly obese subjects had higher levels of total T3 (TT3), FT3, total T4 (TT4), and TSH than those of the control group, probably as a result of the reset of their central thyrostat at higher level (Michalaki, 2006), whereas other researchers showed that in overweight individuals with normal thyroid function the serum TSH levels and the grade of obesity were positively correlated (Michalaki, 2006).

Conclusively, there was a relatively higher prevalence of dysthyroxinaemia in our study even more than in previous studies. However, 2° hypothyroidism happened to be the commonest among the clients in this study which was essentially in contrast with subclinical hypothyroidism found in previous studies. Thyroid function should be encouraged in infertile female clients for proper and prompt management to improve both natural fertility, spontaneous conception as well as conception rates with Assisted Reproductive Therapy.

References

- Aliyu, Y., Adesiyun, A.G., Avidime, S. and Randawa, A.J. (2017). Prevalence of obesity and outcome of weight loss on reproduction. A study among women attending infertility clinic in Zaria, Northern Nigeria. *Archives of Medicine and Surgery*; 2:3-6.
- Araoye, M.O. (2003). Epidemiology of infertility: social problems of the infertile couples. *West African Journal of Medicine*; 22(2): 190-196.
- Cho, M.K. (2015). Thyroid dysfunction and subfertility. *Clinical Experimental Reproductive Medicine*; 42:131-135.
- Dyer, S.J. (2012). The economic impact of infertility on women in developing countries a systematic review. *Facts, View and Vision in Obstetrics and Gynaecology*: 38-45.
- Emokpae, M., Osadolor, H. and Omole, O. (2011). Sub-clinical hypothyroidism in infertile Nigerian women with hyperprolactinaemia. *Nigerian Journal of Physiological Sciences*; 26: 35–38.
- Fupare, S., Jambhulkar, R. and Tale, A. (2015). Correlation of thyroid hormones with infertility in reproductive age group women. *Indian Journal of Basic Applied Medical Research*; 4:488–495.
- Habbu, P.P., Shaikh, A.K. (2016). Study of Thyroid Dysfunction in Association with

- Infertility. *International Journal of Biochemistry Research and Review*; 11: 1–6.
- Iacobellis, G., Ribaudo, M.C., Zappaterreno, A.C., Iannucci, V. and Leonetti, F. Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women. *Clinical Endocrinology*; 62(4): 487–491.
- Kameswaramma, K. (2016). Study of correlation of thyroid profile and clinical parameters in patients with infertility. *International Journal of Reproduction, Contraception, Obstetrics and Gynaecology*; 5:1410-1413.
- Knudsen, N., Laurberg, P., Rasmussen, L.B., Bulow, H.P., Lars, O. and Jorgensen, T. (2005). Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. *Journal of Clinical Endocrinology and Metabolism*; 90(7) 4019–4024.
- Krassas, G.E., Poppe, K. and Glinoer, D. (2010). Thyroid function and human reproductive health. *Endocrinological Review*; 31:702-755.
- Michalaki, M.A., Vagenakis, A.G., Leonardou, A.S., Argentou, M.N., Habeos, I.G., Makri, M.G., Psyrogiannis, A.I., Kalfarentzos, F.E. and Kyriazopoulou, V.E. (2006). Thyroid function in humans with morbid obesity. *Thyroid*; 16(1): 73–78.
- Nasir, S., Khan, M.M., Ahmed, S., Alam, S. and Ziaullah, S. (2016). Role of thyroid dysfunction in infertile women with menstrual disturbances. *Gomal Journal of Medical Sciences*; 14: 20–24.
- Orazulike, N., Odum, E. (2018). Evaluation of thyroid function in infertile female patients in Port Harcourt, Nigeria. *Tropical Journal of Obstetrics and Gynaecology*; 35: 38–42.
- Practice Committee of the American Society for Reproductive Medicine. (2015). Subclinical hypothyroidism in the infertile female population: A guideline. Fertility and Sterility; 104:545-553.
- Poppe, K., Glinoer, D. (2003). Thyroid autoimmunity and hypothyroidism before and during pregnancy. *Human Reproduction Update*; 9:149-161.
- Poppe, K., Velkeniers, B. and Glinoer, D. (2007). Thyroid disease and female reproduction. *Clinical Endocrinology (Oxford)*; 66:309–321.

- Poppe, K., Velkeniers, B. and Glinoer, D. (2008). The role of thyroid autoimmunity in fertility and pregnancy. Endocrinology and Metabolism; 4:394-405.
- Rahman, D., Fatima, P. and Banu, J. (2008). Thyroid Disorders in Female Subfertility. Journal of Chittagong Medical College *Teachers' Association*; 19:46–50.
- Rijal, B., Shrestha, R. and Jha, B. (2011). Association of thyroid dysfunction among infertile women visiting infertility center of Om Hospital, Kathmandu, Nepal. Nepal Medical College Journal; 13: 247–249.
- Sharma, B., Kumar, A., Singh, C. and Kansal, R. (2012). Significance of thyroid profile (serum T3, T4 and TSH) in infertile women. Indian Journal of Clinical Health; 24: 148-152.
- Shivaleela, M., Poornima, R., Amit, D. and Jayaprakash, D. (2012). Thyroid

- Dysfunction in Infertile Women. Research Artic Biological Sciences; 2: 53–58.
- Unuane, D., Tournaye, H., Velkeniers, B. and Poppe, K. (2011). Endocrine disorders and female infertility. Best Practice Research in Clinical Endocrinology and Metabolism; 25(6): 861-873.
- Vayena, E., Rowe, P. and Griffin, P. (2001). Current Practices and Controversies in Assisted Reproduction. Report of a meeting on Medical, Ethical and Social Aspects of Assisted Reproduction held at WHO Headquarters; September, 17-21; Geneva – Switzerland: 2002.
- Verma, I., Sood, P., Juneja, S. and Kaur, S. (2012). Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. International Journal of Applied Basic Medical Research; 2:17-19.

Citation: Biliaminu, S.A., AbdulAzeez, I.M., Khan, N., Bakr, M.R., Oladosu, W.O., Yusuff, J.O. and Okesina, A.B. Dysthyroxinaemia Among Sub-fertile Female Clients Attending Nizamiye Hospital, Abuja, Nigeria. Sokoto Journal of Medical Laboratory Science; 5(4): 4 - 11.

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