Numerical Analysis and Simulation of a Mathematical Modelling on Infertility amongst Male Gender: A Variation Review on Oxidative Stress

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DOI: https://doi.org/10.51584/IJRIAS.2025.100800155

Received: 21 August 2025; Accepted: 28 August 2025; Published: 29 September 2025

ABSTRACT

This study investigated infertility amongst males and the impact of oxidative stress in secretion and concentration of reproductive hormones. The study adopted mathematical modeling with a system of nonlinear first order differential equations. MATLAB ODE45 Numerical Scheme was used for simulations result. The findings revealed that oxidative stress, time delay and negative feedback delay in the concentrations/secretions of luteinizing hormone releasing hormone and Luteinizing hormone made the system to vacillate; the analytic or exact solutions of $H_1(t)$ and $H_2(t)$ showed oscillatory motion in the system; the presence of oxidative stress and negative feedback time lag parameters led testosterone $H_3(t)$ to annihilation; the numerical simulation showed that there is bifurcation and divergent behavior in the system between the hormones as a result of oxidative stress and time delay factors/ parameters; and the amplitude of the oxidative stress in the system is greater than two thousand; from the simulation, the steady state and endemic equilibrium of the model is locally and globally asymptotically unstable due to the impact of oxidative stress and negative feedback on the hormones secretion and concentration showed in figures 4d and 5 respectively. The study is significant to men with hormonal issues, medical practitioners for clinical attention and future researchers will use it as literature review. However, the study recommended that clinical routine checkup should be adhered to by the affected men; efforts should be made to identify and eliminate the sources of reactive oxygen species; antioxidant supplement should be introduced to the affected persons.

Keywords: Oxidative stress; Male infertility; Wave function, Hormones

INTRODUCTION

Infertility is a situation whereby a woman cannot get pregnant after one year and above of trying to conceive. It occurs when a woman is not getting pregnant in the face of having regular and unprotected sex for twelve months and above. Thus, male infertility is a circumstance that affects a man's ability to get his partner pregnant although, treatment could also increase the chances to impregnate his partner. It could result from ovulatory disorders, endometriosis, low sperm count or low testosterone which is the main hormone responsible for male fertility and numerous treatment options are also available for men with infertility problems[33,34]. Nevertheless, studies have shown that oxidative stress could be linked to male infertility resulting to reduced sperm motility, sperm DNA damage and increased risk of recurrent abortions and genetic

diseases**;** but there are several treatment options that are available for men with infertility when diagnosed with [1-10,19,22 28,31,35 39,44 49]. However, oxidative stress negatively affects male reproductive functions and may induce infertility either directly or indirectly by affecting the hypothalamus-pituitary-gonadal (HPG) axis or disrupting its crosstalk with other hormonal axes [20-25]. Oxidative stress reveals an imbalance between the systemic index of reactive oxygen species (ROS) and a natural system's ability to freely cleanse the sensitive intermediates or to repair the resulting damage in male reproductive hormones. Hence, human reproduction is a complex phenomenon and process that involves interactions between many organs. A disruption to the interactive system of a man and woman can result in inability to procreation or have a biological child. Infertility is lack of pregnancy between couples after one of regular unprotected sexual intercourse. Obviously, about 15 –20% of couples in reproductive age are infertile which can be attributed to both male and female factors [41,11,17,18,27,28,30]. Physiologically, time lag rises from the delay caused by the finite time taken in the transmission of messages through nerves or hormones or when populations are distributed over space. As the hypothalamus monitors and causes the release of hormones from the pituitary gland, it arouses the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) into the blood [32-37]. Testosterone is the most important sex hormone in men and it controls fertility, muscle mass, fat distribution, and red blood cell production. When testosterone level drops below the normal levels that are healthy, they can lead to conditions like hypogonadism or infertility [12,13,26,29]. Hormones are chemical substances produced by the glands in the endocrine system. Hormonal imbalances can affect many body functions and can occur naturally at certain points in life when the endocrine glands are not functioning properly [1,43,45,45,]. A variety of several etiological factors including intra-testicular, post-testicular, and external factors, such as alcohol, cigarette smoking, varicocele, diabetes and so on have been correlated with increased levels of ROS and sperm DNA damage which in turn can affect the potentiality of male fertility. Nevertheless, there are other causes of male infertility such as defective sperm function, Reactive oxygen species (ROS), physiological mechanisms, death of spermatozoa, DNA damage in the spermatozoa and so on [14,15,16,29].

MATERIALS AND METHODS

It had been observed that men have a testosterone level of 2.4-12ng/ml of blood, luteinizing hormone is 5-25miu/ml and follicle stimulating hormone of 5- 20miu/ml while women have only 0.2-0.8 ng/ml of testosterone in Nigeria which varies in other countries worldwide [37]. There are many negative feedback pathways in biological systems which can be as a result of time lags factor in male hormones. This includes Temperature regulation, Blood pressure regulation, Blood sugar regulation, Thyroid regulation, Photosynthesis in response to increased carbon dioxide and Predator/prey population dynamic [15,26,37,38,39]. In men, 90 per cent of the total concentration comes primarily from the testis with the rest coming from other parts of the endocrine system which is the reason why women also produce it. Any regular imbalance in testosterone level can cause dramatic personality changes. It is now well recognized that blood testosterone level can fluctuate [43,45,47]. In this work we shall discuss the mathematical presentations of oxidative stress, testosterone time lag in secretion and concentration, and analyze the formulated model by explaining the periodicity of testosterone concentration both analytically and numerically.

Assumptions

1. The study assumed that oxidative stress introduced a lag in the concentrations and secretions of luteinizing hormone releasing hormone or LHRH (H_1) as $A_1\omega\cos(x+kt)$ and for Luteinizing hormone (H_2) as $A_2\omega\sin(x+kt)$ while the Testosterone (H_3) exhibits time delay in its concentration and secretion with t_1, t_2, t_3 and t_4.
2. The negative feedback lag in the concentrations of male hormones is a wave function in the negative x-direction which is a function of amplitude, wavelength, position, velocity and frequency is of the form $\frac{A_1\omega\cos\frac{2\pi}{\lambda}(x+vt)}{P+H_3^n}$ and $\frac{A_2\omega\sin\frac{2\pi}{\lambda}(x+vt)}{P+H_3^n}$.
3. The study assumed that the model can be analyzed analytically to derive conditions for exact solution of the dynamical system and perform numerical simulations to interpret the steady state solution and equilibrium.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VIII August 2025

4. The study used travelling wave equation, $= y(x,t) = ASin\frac{2\pi}{\lambda}(x \pm vt)$, where –vt implies velocity in positive x-direction and where +vt implies velocity in the negative x-direction. Considering the formula, $v = \lambda f$, $v = velocity$, $\lambda = wavelength$, $f = frequency$, $f = \frac{v}{\lambda}$,

The Model Formulation

$$\frac{dH_1}{dt} = -\alpha H_1 + \frac{A_1\omega\cos\frac{2\pi}{\lambda}(x+vt)}{P + H_3^n(t-t_1)} \quad 1$$

$$\frac{dH_2}{dt} = -\beta H_2 + \mu H_1(t-t_2) + \frac{A_2\omega\sin\frac{2\pi}{\lambda}(x+vt)}{P + H_3^n(t-t_3)} \quad 2$$

$$\frac{dH_3}{dt} = -\gamma H_3 + \psi H_2(t-t_4) \quad 3$$

with initial conditions: $H_1(0) = 0$, $H_2(0) = 0$, $H_3(0) = 0$

Table 1: State variables and parameters definitions

State variables	**Definitions**	**Values**	**Source**
$H_1(t)$	Luteinizing hormone releasing hormone		Assumed
$H_2(t)$	Luteinizing hormone		Assumed
$H_3(t)$	Testosterone		Assumed
$\frac{dH_1}{dt}$	Rate of change in Luteinizing hormone releasing hormone w.r.t. t		Das and Roy (1994)
$\frac{dH_2}{dt}$	Rate of change in Luteinizing hormone w.r.t. t		Das and Roy (1994)
$\frac{dH_3}{dt}$	Rate of change in Testosterone hormone w.r.t. t		Das and Roy (1994)
t_1, t_2, t_3, t_4	Time lags <1		Cartwright & Hussain (1986)
Parameters	**Definitions**	**Values**	
α, β, γ	Delay rates in the blood stream in per minutes	$\alpha = 0.1, \beta = .015, \gamma = .023$	Das and Roy (1994)
t	Time independent variable		Cartwright & Hussain (1986)
P, i, n	Are positive constants (i = 1, 2, ….), $P > 0$, $n > 1$	$\mathbf{1\frac{ng}{ml}/min}$	Das and Roy (1994)
A_1, A_2	Amplitude of open loop gain of feedback in the negative x-direction a function of frequency	1,2,…	Estimated
H_3^m	The gain of feedback path for testosterone, a function of frequency		Das and Roy (1994)
M	gain of feedback path for testosterone	1,2,3,4,5	Das and Roy (1994)
μ, ψ	Rates of production of $H_2(t)$ and $H_3(t)$		Das and Roy (1994)
$sin\frac{2\pi}{\lambda}(x+vt)$	The open loop gain of feedback in the negative x-direction a function of frequency		Assumed
v	velocity in the open loop gain of feedback in the negative x-direction		Assumed
λ	Wavelength in the open loop gain of feedback in the negative x-direction		Estimated

x	Position of the hormone in the open loop gain of feedback in the negative x-direction		Estimated
$2\pi x$	Perimeter of the open loop gain of feedback in the negative x-direction		Assumed
$sin(x-kt)$	Effect of oxidative stress on Luteinizing hormone, H_2		Estimated
$cos(x-kt)$	Effect of oxidative stress on Luteinizing hormone releasing hormone , H_1		Estimated
k		0.5	Assumed
A_1, A_2	Amplitude of oxidative stress on H_1 and H_2	1	Estimated
σ	Oxidative stress in the sperm cells (KN)		Murray (1989)
τ	Traction force generated by the cell	0.7	Murray (1989)
ρ	Density of sperm cells in the testis	1.2×10^{-2}	Agarwal et al. (2021)
λ	Measure of force activation resulting from the neighbouring cells	30	Nedresky & Singh (2021)
I	unit stress tensor	0.3	Murray (1997)
x	Position of the sperm cells in 3–dimension	2.1	Estimated
k	Rate of destruction of sperm cells	0.5	Agarwal, et al. (2014)
γ	Measure of the nonlocal long range cell in the testis	0.5	Murray (1997)
$\boldsymbol{\omega}$		$\boldsymbol{\frac{2\pi}{12}}$	Assumed

From equation (1)

$$\frac{dH_1}{dt} = -\alpha H_1 + \frac{A_1\omega\cos\frac{2\pi}{\lambda}(x+vt)}{P+H_3^m(t-t_1)} \qquad 1$$

IF $e^{\alpha dt} = e^{\alpha t}$

$$\left(H_1^{'} + \alpha H_1\right)e^{\alpha t} = \frac{A_1\omega\cos\frac{2\pi}{\lambda}(x+vt)}{P+H_3^m(t-t_1)}e^{\alpha t}$$

$$\frac{d\left(H_1 e^{\alpha t}\right)}{dt} = \frac{A_1\omega\cos\frac{2\pi}{\lambda}(x+vt)}{P+H_3^m(t-t_1)}e^{\alpha t}$$

Upon integration by parts, we have

$$\int udv = uv - \int vdu$$

$$u = \cos\frac{2\pi}{\lambda}(x+vt), \qquad dv = e^{\phi t}, \qquad v = \frac{e^{\alpha t}}{\alpha}$$

$$du = -vsin(x+vt)$$

Put: $\int e^{\alpha t}\cos\frac{2\pi}{\lambda}(x+vt)dt = I$

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VIII August 2025

$$H_1 e^{\phi t} = \frac{A_1 \omega}{P} I$$

$$I = \frac{e^{\alpha t}}{\alpha} \cos \frac{2\pi}{\lambda}(x + vt) + \int \frac{v}{\alpha} \sin \frac{2\pi}{\lambda}(x + vt) e^{\alpha t} dt$$

$$u = sin\,\tfrac{2\pi}{\lambda}(x + vt),\ dv = e^{\phi t},\ v = \frac{e^{\alpha t}}{\alpha}$$

$$du = v cos \frac{2\pi}{\lambda}(x + vt)$$

$$= \frac{e^{\alpha t}}{\alpha} \cos \frac{2\pi}{\lambda}(x + vt) + \frac{v}{\alpha^2} \sin \frac{2\pi}{\lambda}(x + vt) e^{\alpha t} - \frac{v^2}{\alpha^2} \int \cos \frac{2\pi}{\lambda}(x + vt) e^{\alpha t} dt$$

$$= \frac{e^{\alpha t}}{\alpha} \cos \frac{2\pi}{\lambda}(x + vt) + \frac{v}{\alpha^2} \sin \frac{2\pi}{\lambda}(x + vt) e^{\alpha t} - \frac{v^2}{\alpha^2} I$$

$$I\left(1 + \frac{v^2}{\alpha^2}\right) = \frac{e^{\alpha t} \cos \frac{2\pi}{\lambda}(x + vt)}{\alpha} + \frac{v}{\alpha^2} \sin \frac{2\pi}{\lambda}(x + vt) e^{\alpha t} + G \qquad (3.19)$$

$$I = \frac{\alpha e^{\alpha t}}{v^2 + \alpha^2} \cos \frac{2\pi}{\lambda}(x + vt) + \frac{v e^{\phi t}}{\alpha^2 + v^2} \sin \frac{2\pi}{\lambda}(x + vt) + G \qquad (3.20)$$

$$\Rightarrow H_1 e^{\alpha t} = \frac{A_1 \omega}{P} \frac{\alpha e^{\alpha t}}{v^2 + \alpha^2} \cos \frac{2\pi}{\lambda}(x + vt) + \frac{A_1 \omega}{P} \frac{v e^{\phi t}}{\alpha^2 + v^2} \sin \frac{2\pi}{\lambda}(x + vt) + G$$

$$H_1(t) = \frac{A_1 \omega}{P} \frac{\alpha}{v^2 + \alpha^2} \cos \frac{2\pi}{\lambda}(x + vt) + \frac{A_1 \omega}{P} \frac{v}{\alpha^2 + v^2} \sin \frac{2\pi}{\lambda}(x + vt) + G e^{-\alpha t} \qquad 3.22$$

Initial condition $H_1(0) = Q(constant)$

Using equation (3.22) gives

$$Q = \frac{A_1 \omega}{P} \frac{\alpha}{v^2 + \alpha^2} \cos \frac{2\pi}{\lambda} x + \frac{A_1 \omega}{P} \frac{v}{\alpha^2 + v^2} \sin \frac{2\pi}{\lambda} x + G$$

$$G = Q - \frac{A_1 \omega}{P} \frac{\alpha}{v^2 + \alpha^2} \cos \frac{2\pi}{\lambda} x - \frac{A_1 \omega}{P} \frac{v}{\alpha^2 + v^2} \sin \frac{2\pi}{\lambda} x$$

$$H_1(t) = \frac{A_1 \omega}{P + H_3^m(t - t_1)} \frac{\alpha}{v^2 + \alpha^2} \cos \frac{2\pi}{\lambda}(x + vt) + \frac{A_1 \omega}{P + H_3^m(t - t_1)} \frac{v}{\alpha^2 + v^2} \sin \frac{2\pi}{\lambda}(x + vt) +$$

$$Q e^{-\alpha t} - \frac{A_1 \omega}{G + H_3^m(t - t_1)} \frac{\alpha e^{-\alpha t}}{v^2 + \alpha^2} \cos \frac{2\pi x}{\lambda} + \frac{A_1 \omega}{P + H_3^m(t - t_1)} \frac{\alpha e^{-\alpha t}}{v^2 + \alpha^2} \sin \frac{2\pi x}{\lambda} \qquad 3.23$$

Similarly, from equ (2) we have

$$\frac{dH_2}{dt} = -\beta H_2 + \mu H_1(t - t_2) + \frac{A_2 \omega \sin \frac{2\pi}{\lambda}(x + vt)}{P + H_3^m(t - t_3)} \qquad 3.24$$

$$H_2(t)=\frac{A_1\omega}{P+H_3^m(t-t_3)}\frac{\alpha}{v^2+\alpha^2}\sin\frac{2\pi}{\lambda}(x+vt)-\frac{A_1\omega}{P+H_3^m(t-t_3)}\frac{v}{\alpha^2+v^2}\cos\frac{2\pi}{\lambda}(x+vt)+$$
$$Ge^{-\alpha t}-\frac{A_1\omega}{P+H_3^m(t-t_3)}\frac{\alpha e^{-\alpha t}}{v^2+\alpha^2}\cos\frac{2\pi x}{\lambda}+\frac{A_1\omega}{P+H_3^m(t-t_3)}\frac{\alpha e^{-\alpha t}}{v^2+\alpha^2}\sin\frac{2\pi x}{\lambda} \quad 3.25$$

Finally, equ (3) gives $H_3(t)=0$ under initial condition, this implies that time delay has serious negative impact on the testosterone hormone secretion and concentration in men. Considering the impact of oxidative stress tensor σ_{cell} as an activator of hormonal impairment in men makes more cells to damage and pack up leading to cell tractions for greater traction force. This implies that cell-cell contact activation increases traction force for large damaged sperm cell densities. Assuming that the cell traction forces, $\tau(n)$ per unit mass of matrix, initially increases with m and increases with m for very large m. we have

$$\tau(n)=\frac{n\tau}{1+\lambda n^2} \quad 3.26$$

where τ is the traction force generated by the cell, n is the number of sperm cells in the body and λ is the measure of force activation resulting from the neighbouring cells. For the cell traction oxidative stress (σ_{Cell}) we have

$$\sigma_{cell}=n\tau\rho(N-n)I \quad 3.27$$

where τ is the cell traction, I is the unit tensor, ρ is the sperm cell density, $n=n(x,t)$ is the number of damage cells packed within the testis, male genital tract, or after ejaculation in the seminal fluid and N (injured steady state) controls the activation of cell traction as the cell density increases. Sperm cell damage can also be a result of infections, varicocele (swollen veins in the scrotum) or oxidative stress. For this study, considering the contribution of σcell to oxidative stress tensor Murray, (1989) we have

$$\sigma_{cell}=\frac{n\tau}{1+\lambda n^2}\left(\rho+\gamma\nabla^2\rho\right)I \quad 3.28$$

where $\gamma>0$ is the measure of the nonlocal long range cell –testis. Considering that the damaged cells are densely packed equation (3.28) becomes

$$\sigma_{cell}=\frac{\tau\rho}{1+\lambda n^2}\left(n+\gamma\nabla^2 n\right)I \quad 3.29$$

$$\sigma=\frac{\tau\rho}{1+\lambda(x_i-kt)^2}\left(I(x_i-kt)+3\gamma I(x_i-kt)^2\right) \quad 3.30$$

Equation (3.30) is the Oxidative Stress in the sperm cell.

Numerical Simulations

The graphical solutions showed the secretion and concentration of the male reproductive hormones measuring *in* milli-international units per milliliter (miu/ml) and nanograms per milliliter (ng/ml) against Time in minutes; and the oxidative stress in Kilo Newton with respect to time in days. The Parameter values are: $A_1=A_2=0.6,1\ldots$, $\omega=0.4$, $k=0.5$, $x=1$, $t=0:5:100$,

$H_1=0:5:100$, $H_2=0:5:100$, $H_3=0:5:100$, $m=4$, $t_1=t_2=t_3=t_4=0$, $A=B=1\frac{ng}{ml}/min$, $\mu=5$ *and* $\lambda=.01\ min^{-1}$, $\alpha=.1,\beta=.015,\gamma=.023$ in per mins

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VIII August 2025

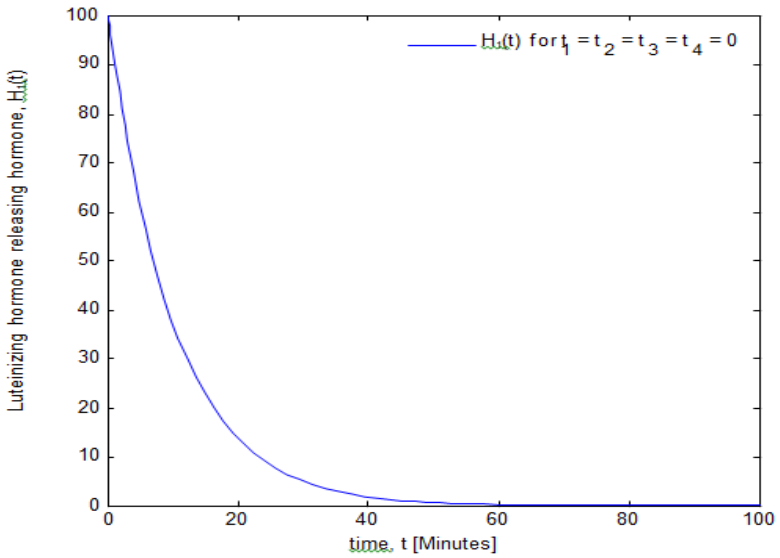

Figure 1 Luteinizing hormone releasing hormone $H_1(t)$in milli-international units per milliliter (miu/ml)against Time in minutes

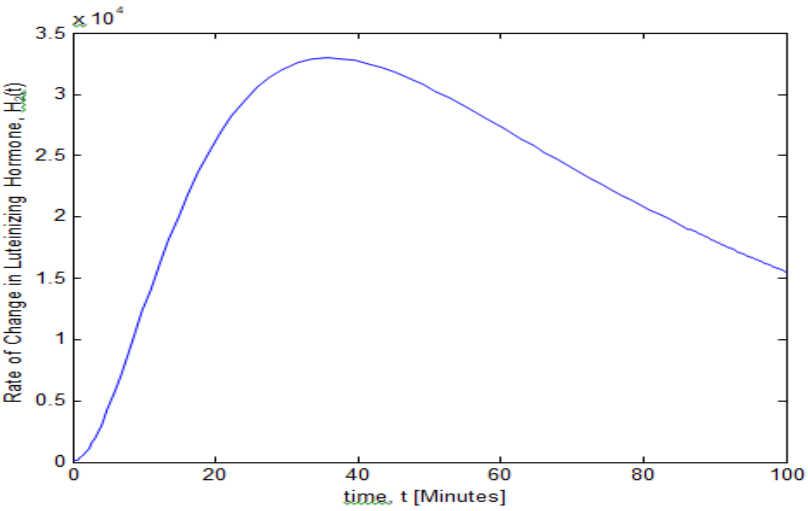

Figure 2 Luteinizing hormone, $H_2(t)$in milli-international units per milliliter (miu/ml) against Time in Minutes. Parameter values are: $A_1 = A_2 = 1$, $\omega = \frac{2\pi}{12}$, $k = 0.5$, $x = 1$, $t = 0:5:100$, $X = 0:5:100$, $Y = 0:5:100$, $Z = 0:5:100$, $m = 5$, $t_1 = t_2 = t_3 = t_4 = 0$

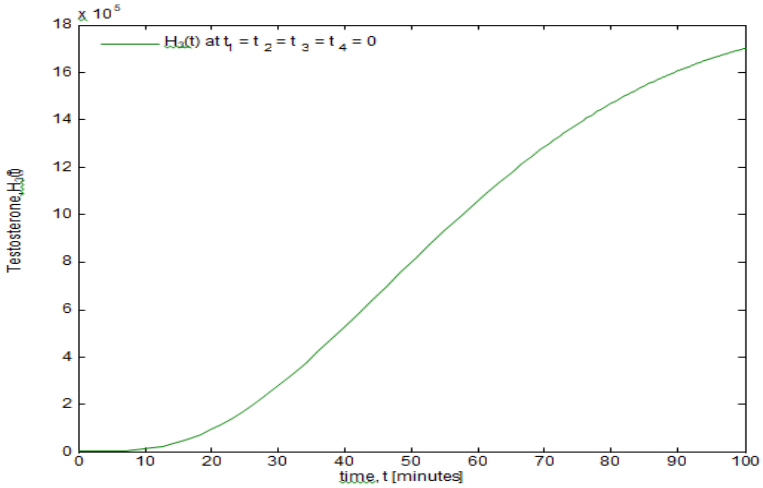

Figure 3 Testosterone $H_3(t)$in nanograms per milliliter (ng/ml) against Time in Minutes Parameter values are: $A_1 = A_2 = 1$, $\omega = \frac{2\pi}{12}$, $k = 0.5$, $x = 1$, $t = 0:5:100$, $H_3 = 0:5:100$, $m = 5$, $t_1 = t_2 = t_3 = t_4 = 0$,

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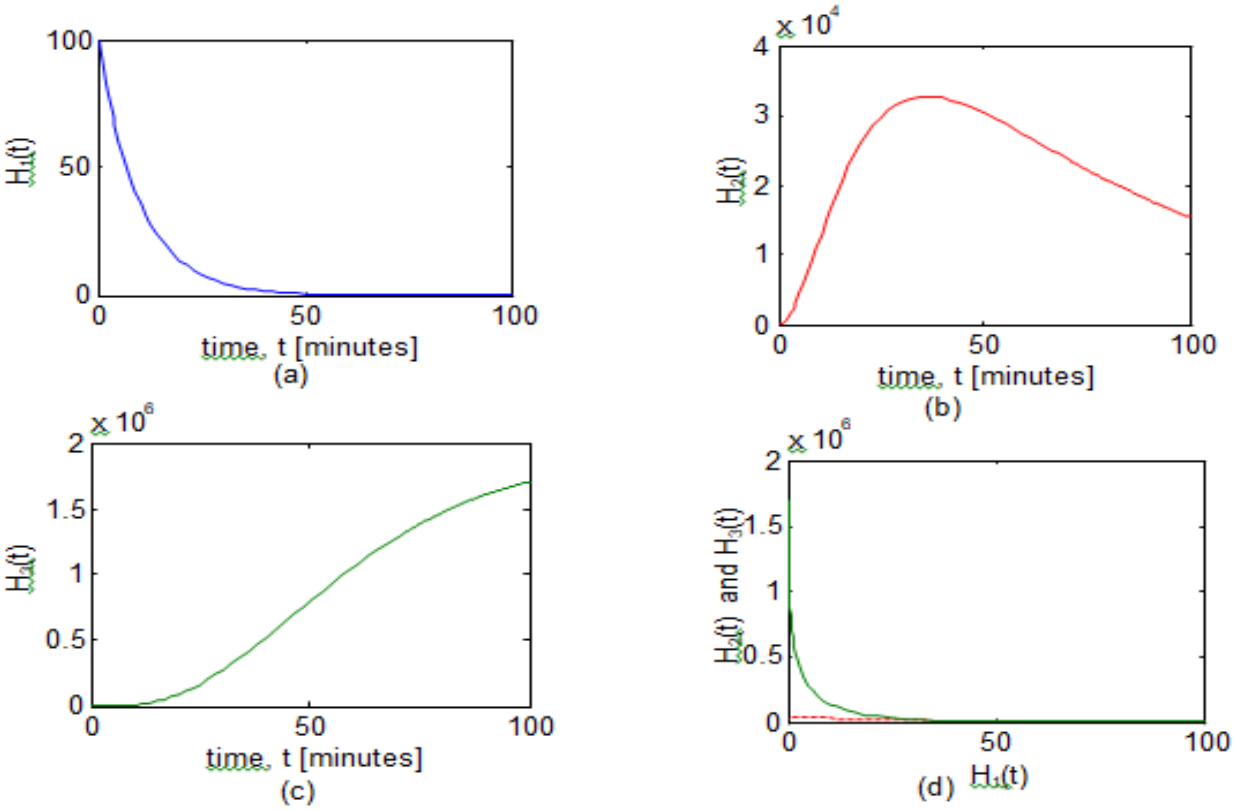

Figure 4: (a) Luteinizing hormone releasing hormone $H_1(t)$ against Time, t, (b) Luteinizing hormone, $H_2(t)$ against Time, (c) Testosterone $H_3(t)$ against Time and (d) Luteinizing hormone $H_2(t)$ and Testosterone $H_3(t)$ against Luteinizing hormone releasing hormone $H_1(t)$ with parameter values: $A_1 = A_2 = 1$, $\omega = \frac{2\pi}{12}$, $k = 0.5$, $x = 1$, $t = 0:5:100$, $H_1 = 0:5:100$, $H_2 = 0:5:100$, $H_3 = 0:5:100$, $m = 5$, $t_1 = t_2 = t_3 = t_4 = 0$, $P = B = 1\frac{ng}{ml}/min$, $\mu = 5$ and $\lambda = .01\ min^{-1}$, $\alpha = .1, \beta = .015, \gamma = .023$ in per mins

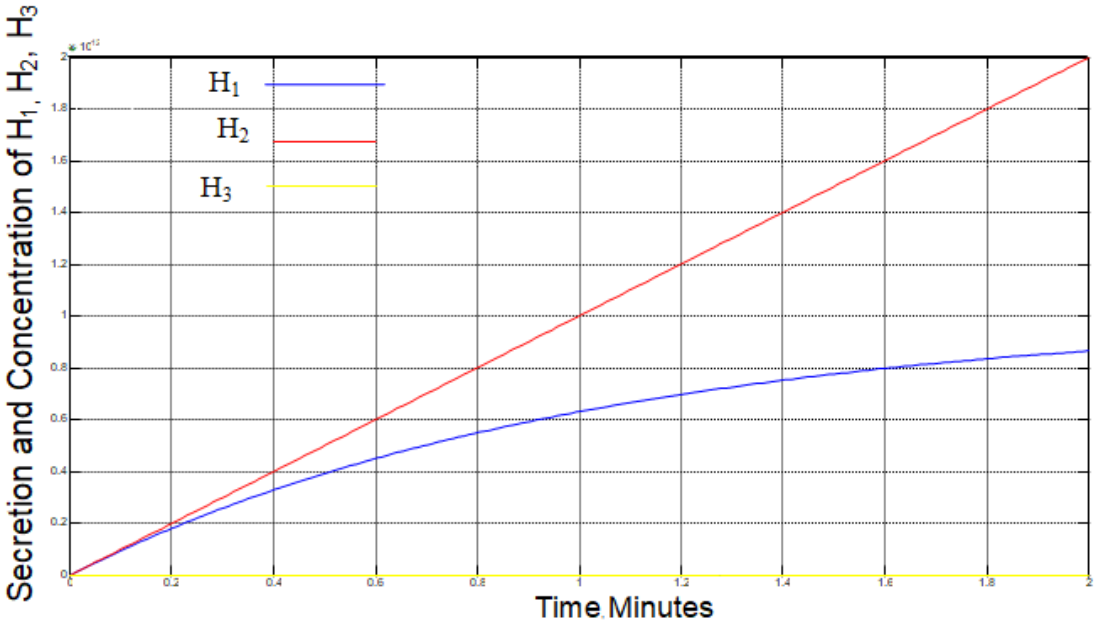

Figure 5 showed bifurcation and divergence in the secretion and concentration of the Luteinizing hormone releasing hormone (H_1), Luteinizing hormone (H_2) and Testosterone (H_3) against Time in minutes with parameter values: $A_1 = A_2 = 1$, $\omega = \frac{2\pi}{12}$, $k = 0.5$, $x = 1$, $t = 0:5:100$, $H_1 = 0:5:100$, $H_2 = 0:5:100$, $H_3 = 0:5:100$, $m = 5$, $t_1 = t_2 = t_3 = t_4 = 0$, $P = B = 1\frac{ng}{ml}/min$, $\mu = 5$ and $\lambda = .01\ min^{-1}$, $\alpha = .1, \beta = .015, \gamma = .023$ in per mins

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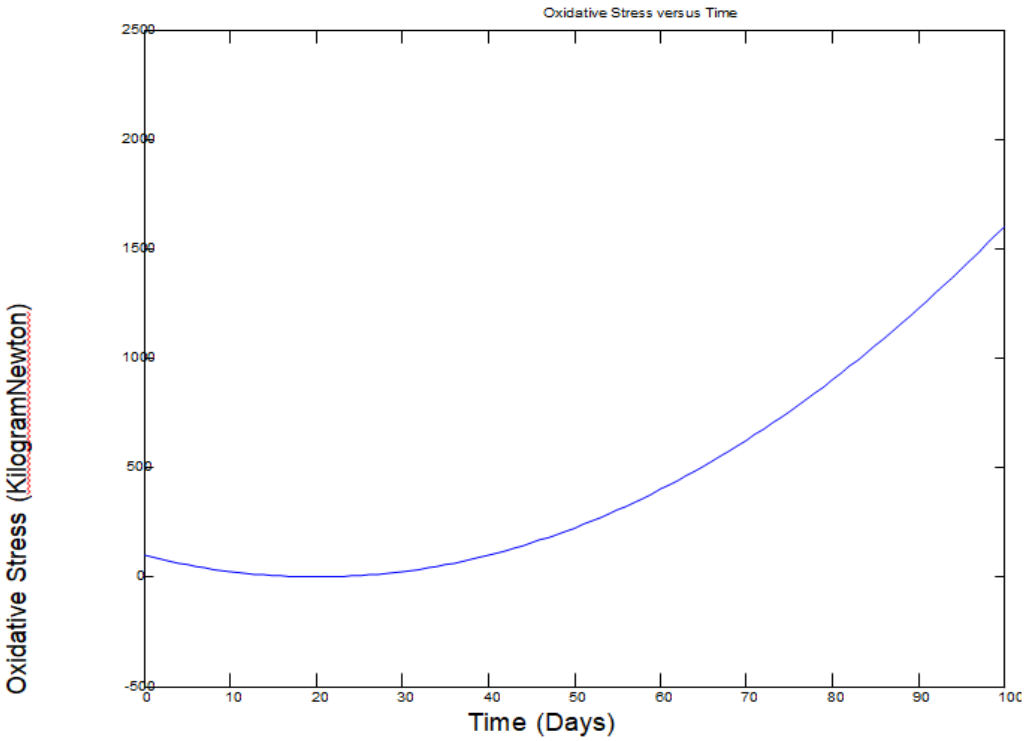

Figure 6 shows shows the action of oxidative stress in the hormones against time in days

Values: $\tau = 0.7$, $\rho = 1.2 \times 10^{-2}$, $\lambda = 30$, $I = 0.3$, x = 2.1 $k = 0.5$, $\gamma = 0.5$, $t = 0:5:100$

This graph shows an exponential rise in nature, which means that oxidative stress rises negatively against the hormones with respect to time. This phenomenon indicates that it has indicial pattern which could lead to oscillation of the hormones under some varying parameters. Also, this depicts that oxidative stress has lost its connection power in body of the male organism thereby increasing fertility impairment by affecting the Luteinizing hormone releasing hormone $\boldsymbol{H_1(t)}$, Luteinizing hormone $\boldsymbol{H_2(t)}$ and Testosterone $\boldsymbol{H_3(t)}$ as reflected in figure 4d. It also showed that as the time increases in days, the action of oxidative stress increases monotonically with the amplitude of stress in the hormone 2200KN at three months and plus or minus 100days.

DISCUSSION AND INTERPRETATION OF THE RESULTS

The model exact solutions from equations (1 –2) showed an exponential increase and quadratic in velocity in the open loop gain of feedback in the negative x-direction and rates of delay in the blood stream; while equation (3) approaches to zero using the initial conditions. The mechanisms of male fertility impairment were reduced sperm motility, sperm DNA damage and increased risk of recurrent abortions and genetic diseases. The study revealed that oxidative stress time delay with the negative feedback delay in the concentrations and secretions of luteinizing hormone releasing hormone and Luteinizing hormone made the system to vacillate. The analytic or exact solutions of $\boldsymbol{H_1(t)}$ and $\boldsymbol{H_2(t)}$ showed oscillations of sine, cosine and exponential functions. The result also showed that due to the presence of oxidative stress and negative feedback time lag parameters, testosterone $H_3(t)$ was annihilated and reduces to zero completely. Figure 1 showed that $H_1(t)$ decreases exponentially and approaches zero as time increases which describes unstable phenomenon. Figure 2 illustrates a monotone rise to the tip with a sharp descent indicating that it does not support dominance. Figure 3 showcased that $H_3(t)$when the time lag is zero increases monotonically to be sustained but the action of oxidative stress makes it to collapse easily without reproducing. Figure 4d showing the Luteinizing hormone $H_2(t)$ and Testosterone $H_3(t)$ against Luteinizing Hormone Releasing Hormone $H_1(t)$ explains the impact of oxidative stress and time lags in the system thereby showing a nonlinear interaction. The numerical simulation of figure 4 & 5 showed that it bifurcates and diverges in the oozing of the hormones secretion and concentration in the system as a result of oxidative stress and time delay factors/ parameters. It also showed that the amplitude of the oxidative stress in the system is above 1500KN at time three months and some days.

From biological point of view, the study revealed that oxidative stress is the major foundation of male infertility which generates disparity amid reactive oxygen species (ROS) and antioxidants, causing damage of proteins, lipids and sperm DNA. However, low level of ROS is essential for sperm function while too much of ROS from factors like diet, lifestyle, varicocele, inflammation, genetic factors, hormonal imbalances can blight sperm motility, morphology and DNA integrity. This damage makes the sperm's ability to fertilize an egg unproductive and that contributes to male infertility. Based on these facts, the resulting consequences are Reduced sperm motility and viability, Impaired sperm function, Increased DNA damage which reduces pregnancy rates after assisted reproductive techniques like intrauterine insemination, Compromised sperm maturation and Decreased overall reproductive function. These findings are in conformity with the results obtained by [18,20,50,51,52] on male hormones and oxidative stress. This study did not cover clinical validation, systematical stability analysis, existence and uniqueness of the solution.

CONCLUSION/RECOMMENDATIONS

In conclusion, the solutions showcased that oxidative stress and negative feedback identified in this study impaired the male reproductive hormones negatively by making the releasing hormone and luteinizing hormone in a man to fluctuate without pregnancy. When the simulation is carried out the concentration and secretion of $\boldsymbol{H_1(t)}$ and $\boldsymbol{H_2(t)}$ oscillate over time without any success due to the absence of $H_3(t)$. This revealed that oxidative stress and negative feedback are asymptotically on the increase eating deep into the hormones from the simulation while $\boldsymbol{H_3(t)}$ which is the main hormone goes to extinction without been recovered. In this model, when oxidative stress and negative feedback terms are considered in the system for the oscillatory waves (oscillations) of the hormones involved in the system of interactions become clearer and each monotonically increase the intensity of secretion experienced in the whole system while testosterone monotonically decreases to zero in the whole system. However, the findings are related to [15, 47, 22, 36]

Ethical Statement: There was no direct patients' data involved in this study.

Conflict of Interest: The authors declared that there is no conflict of interest. They all agreed to self-sponsor and paid for the article publication fee.

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