ISSN (e): **2250 – 3005** || Vol, 04 || Issue, 8 || August – 2014 ||
International Journal of Computational Engineering Research (IJCER)

Stochastic Model to Find the Diagnostic Reliability of Gallbladder Ejection Fraction Using Normal Distribution

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Abstract: *To assess the diagnostic reliability of gallbladder ejection fraction in patients with suspected biliary pain. For a class of nonlinear diffusion equations we use the Painleve analysis. In some cases we find that it has only the conditional Painleve property and in other cases, just the painleve property. We also obtained special solutions of Painleve analysis. In that, one of the solution (i.e) the reduction of nonlinear diffusion equation to Riccati equation was used for the gallbladder ejection fraction.*

Key Words: *Gallbladder Ejection Fraction, Normal Distribution, Painleve Property, Riccati Equation, Cholecystokinin, Chronic Acalculous Cholecystitis.*

2010 Mathematics Subject Classification: *60H99, 60G99*

1. Introduction:

Measurement of gallbladder emptying with either oral fatty meal or intravenous administration of octapeptide of cholecystokinin (CCK-8) is a standard procedure in the evalution of patients with varieties of gallbladder diseases. When quantitative cholescintigraphy was introduced nearly 30 years ago, 10ng/kg of CCK-8 was infused intravenously over a three minute period and an ejection fraction value of 35% or greater was considered as normal. Intravenous infusion of CCK-8 has become more popular than ingestion of a fatty meal.

Quantitative cholescintigraphy is critical in the evalution of hepatobiliary diseases [5], and biliary dyskinesia**.** Since biliary dyskinesia is purely a functional abnormality, traditional method of correlation with other imaging test such as ultrasound does not appear appropriate, and therapeutic outcome studies become critical for assessment of accuracy of diagnostic techniques. We undertook the current study in fairly large number of patients with abdominal pain to find out the therapeutic outcome results by infusing CCK-8 for three minutes. Merit of any diagnostic test depends upon its ability to separate normal subjects from those with the underlying disease [4].

In recent years, much attention has been focused on higher order non linear partial differential equations, known as evolution equations. Such nonlinear equations often occur in the description of chemical and biological phenomena. Their analytical study has been drawing immense interest. In [1], a nonlinear partial differential equation is integrable if all its exact reductions to ordinary differential equations have the Painleve property: that is, to have no movable singularities other than poles.

This approach poses an obvious operational difficulty in finding all exact reductions. The reduction of $u_t = \mu u^2 u_x + Du u_{xx} + Du_x^2$ to Riccati equation was used to find the gallbladder ejection fraction.

2. Notations:

$GBCF$	-	Gallbladder Ejection Fraction
$CCK-8$	-	Cholecystokinin
β	-	Intensity
φ	-	Arbitrary Function
r_j	-	Resonances

A	-	Shape Parameter
B	-	Scale Parameter

3. Painleve Analysis:

In [1], a nonlinear partial differential equation is integrable if all its exact reductions to ordinary differential equations have the Painleve property: that is, to have no movable singularities other than poles. This approach poses an obvious operational difficulty in finding all exact reductions. This difficulty was circumvented by [12] by postulating that a partial differential equation has the Painleve property if its solutions are single - valued about a movable singular manifold

$$\varphi(z_1, z_2, \dots, z_n) = 0$$

where φ is an arbitrary function. In other words, a solution $u(z_i)$ of a partial differential equation should have a Laurent - like expansion about the movable singular manifold $\varphi = 0$:

$$u(z_i) = [\varphi(z_i)]^{\alpha} \sum_{j=0}^{\infty} u_j(z_i)\varphi(z_i)^j \tag{1}$$

where α a is a negative integer. The number of arbitrary functions in expansion (1) should be equal to the order of the partial differential equation. Inserting expansion (1) into the targeted equation yields a recurrence formula that determines $u_n(z_i)$ for all $n > 0$, except for a finite number of $r_1, r_2, \dots, r_j > 0$, called resonances. For some equations, the recurrence formulas at the resonance values may result in constraint equations for the movable singular manifold which implies that it is no longer completely arbitrary. In such cases, one can say that the equation has the Conditional Painleve Property [6]. The Painleve property is a sufficient condition for the integrability or solvability of equations. Meanwhile, various authors have applied this approach to other nonlinear partial differential equations to decide whether or not these equations are integrable. Recent investigations of [2] regarding the Painleve analysis also yield a systematic procedure for obtaining special solutions when an equation possesses only the conditional Painleve property. From [3] proposed the nonlinear diffusion equation

$$u_t = Du_{xx} + \beta u(1-u) \tag{2}$$

as a model for the propagation of a mutant gene with an advantageous selection of intensity β. From [6] has considered the extended form of equation (2) as

$$u_t = \beta u^p(1-u^q) + D(u^m u_x)_x \tag{3}$$

For Painleve analysis and obtained special solutions for various cases of p, q and m.

In this paper we consider

$$u_t = \beta u^p(1-u^q) + \mu u^s u_x + D(u^m u_x)_x \tag{4}$$

This is a generalization of (3) for the Painleve analysis. This equation has several interesting limiting cases which have already been studied:

(i) When $\mu = m = 0, p = 1$ and $q \neq 0$, equation (4) is reduced to the generalized Fisher equation. For $q = 1$, equation (4) reduces to the Fisher equation and for $q = 2$, (4) reduces to the Newell Whitehead equation.

(ii) If we take $\beta = m = 0$, then equation (4) is reduced to the generalized Burgers equation. With $s = 1$ and $\beta = m = 0$, equation (4) gives the Burgers equation, which describes the far field of wave propagation in nonlinear dissipative systems [13].

(iii) When $m = 0, p = 1$ and $q = s$, equation (4) is reduced to the generalized Burger - Fisher equation [11].

The behavior of solutions of equation (4) at a movable singular manifold,

$$\varphi(x,t) = 0$$

is determined by a leading order analysis where by one makes the substitution

$$u(x,t) = u_0(x,t)[\varphi(x,t)]^{\alpha} \tag{5}$$

and balances the most singular or dominant terms. Substituting (5) into (4), we obtain three possible values for α as follows:

Case (i):

$p + q > m \geq s$: Balancing the dominant terms $u^{p+q}, mu^{m-1}u_x^2$ and $u^m u_{xx}$, we obtain

$$\alpha = -2/(p+q-m-1) \tag{6}$$

and

$$\beta u_0^{p+q-m-1} = 2D(p+q+m+1)\varphi_x^2/(p+q-m-1)^2$$

Case (ii):

$p+q > s > m = 0$: Balancing the dominant terms u^{p+q} and $u^s u_x$, we obtain

$$\alpha = -1/p+q-s-1$$

and

$$\beta u_0^{p+q-s-1} = (-\mu/p+q-s-1)\varphi_x$$

For $p+q = -m+2s+1 > s > m$,

$$\alpha = -1/(s-m) \tag{7}$$

Here we have two branches for u_0 as follows:

Branch (i): $u_0 = -(k+1)\varphi_x$ & Branch (ii): $u_0 = k\varphi_x$ where $k = 1, 2, 3, \ldots$

$$m = ((2k+1)^2 - 9)/4 \text{ and } \beta = \mu = D = 1 \tag{8}$$

Case (iii):

$s > m \geq p+q$: Balancing the dominant terms $u^s u_x, mu^{m-1}u_x^2$ and $u^m u_{xx}$, we obtain

$$\alpha = -1/(s-m)$$

and

$$u_0^{s-m} = (D/\mu)((1+s)/(s-m))\varphi_x \tag{9}$$

We have the following lemma as a result.

Lemma:

For all combinations of integer values of p, q, m and s, the leading order singularity of equation (4) is

(i) A movable pole for all combinations with $(p+q-m-1)$ is equal to 1 or 2 for case (i), with $(p+q-s-1)$ being equal to 1 for case (ii), and with $s-m$ being equal to 1 for case (iii).

(ii) A rational branch point for all combinations with $(p+q-m-1) > 2$ for case (i). $(p+q-s-1) > 1$ for case (ii) and $s-m > 1$ for case (iii).

The powers of φ, at which the arbitrary coefficient appears in the series, that is, the resonances are determined by setting

$$u(x,t) = u_0(x,t)\big(\varphi(x,t)\big)^{\alpha} + p\big(\varphi(x,t)\big)^{\alpha+r}$$

and balancing the most singular terms of equation (4) again. We obtain for case (i), using the value of α given by (6),

$$p\{(r+\alpha)^2 + (2m\alpha - 1)(r+\alpha)[m\alpha(\alpha-1) + m(m-1)\alpha^2 - 2(p+q)(p+q+m+1)/(p+q-m-1)^2]\} = 0$$

with solutions

$$r = -1, \quad 2[1 - \alpha(m+1)]$$

However, for case (ii), with value α given in (7) and for a particular value of m given by (8), we obtain for branch (i)

$$p\{(2m\alpha(r+\alpha) + \alpha^2 m(m-1) + (r+\alpha)(r+\alpha-1) + \alpha(\alpha-1)m) - \big(s\alpha + (r+\alpha)\big)(k+1) - (-m+2s+1)(k+1)^2\} = 0$$

with solutions

$$r = -1, \quad (k+3) - 2\alpha(m+1)\}$$

and for branch (ii)

$p\{(2m\alpha(r+\alpha)+\alpha^2 m(m-1)+(r+\alpha)(r+\alpha-1)+\alpha(\alpha-1)m)+(s\alpha+(r+\alpha))k+(-m+2s+1)k^2\}=0$

with solutions
$r=-1\ \&\ (2-k)-2\alpha(m+1)$

For case (iii), we get

$$p\{r^2+r(2\alpha(m+1))-r+\alpha^2(1+m)^2-\alpha(1+m)+\alpha s(r+\alpha)u_0^{s-m}\}=0$$

with solutions

$$r=-1\ \&\ -\alpha(1+s) \tag{10}$$

By using the above lemma, we consider the following cases;

(i) $m=0, s=0, p=1, q=2$

(ii) $m=0, s=1, p=1, q=2$

(iii) $m=0, s=1, p=0, q=0$

(iv) $m=1, s=2, p=0, q=0$

(v) $m=2, s=3, p=q=1,$

In which equation (4) has a movable pole as leading order singularity, and therefore, it may have a valid Laurent Expansion.
Now consider the case (iv): Equation (4) with $m=1, s=2, p=q=0$

In this case, equation (4) becomes

$$u_t=\mu u^2 u_x+Duu_x+Du_x^2 \tag{11}$$

Using (9) and (10), we obtain

$$u_0=(3D/\mu)\varphi_x$$

and the resonances are $r=-1$ and 3. Hence, we take the Laurent expansion of the form

$$u=u_0\varphi^{-1}+u_1+u_2\varphi+u_3\varphi^2 \tag{12}$$

Substituting (12) into (11) and collecting coefficients of equal powers of φ, we have

$$\varphi^{-4}:\quad u_0=(3D/\mu)$$
$$\varphi^{-3}:\quad u_1=0$$
$$\varphi^{-2}:\quad u_2=(-1/3D)\sigma_t$$
$$\varphi^{-1}:\quad 0Xu_3=0 \tag{13}$$

Equation (13) shows that u_3 is an arbitrary function. Therefore (11) possesses the Painleve property.

4. Reduction of $u_t=\mu u^2 u_x+Duu_x+Du_x^2$ to Riccati Equation:

Let $u=f(z)$, where

$$z=x-ct \tag{14}$$

Substituting (14) into (11) with $\mu=D=1$ we obtain

$$cf'+f^2f'+ff''+f'^2=0 \tag{15}$$

Integrating (15) once, we get

$$f'=-(c+(f^2/3)) \tag{16}$$

Equation (16) is a Riccati Equation, which can be linearized through the transformation

$$f=3y'/y \tag{17}$$

Substituting (17) into (16), we get

$$y''=(-c/3)y(z) \tag{18}$$

which is a second order linear differential equation. Solving (18), we obtain

$$y(z) = A\cos\sqrt{(c/3)}z + B\sin\sqrt{(c/3)}z \tag{19}$$

Using (19) then (17) becomes

$$f(z) = \sqrt{3c}\left(\left(-A\sin\sqrt{(c/3)}z + B\cos\sqrt{(c/3)}z\right)/\left(A\cos\sqrt{(c/3)}z + B\sin\sqrt{(c/3)}z\right)\right) \tag{20}$$

5. Example:

Total of 140 subjects (113 women, 27 men) with a mean age of 46 years were selected retrospectively from a list of 444 patients. Hepatic extraction fraction and excretion halftime were determined as described [5]. Differential hepatic bile flow into gallbladder versus small intestine was calculated by dividing the total gallbladder counts by the sum of gallbladder and small intestinal counts at 60 minutes after radiotracer injection. Gallbladder phase study was obtained separately between 61 to 90 minutes by collecting data on the same size computer matrix at one frame/minute. Octapeptide of cholecystokinin (CCK-8), 10ng/kg, was infused over three minutes through an infusion pump, infusion beginning at 65 minutes after radiotracer injection (Figure 1). Gallbladder ejection fraction (GBEF) was calculated in the standard fashion [4] & [7-10].

Figure 1: In a normal subject, the gallbladder empties with an ejection fraction of 59%

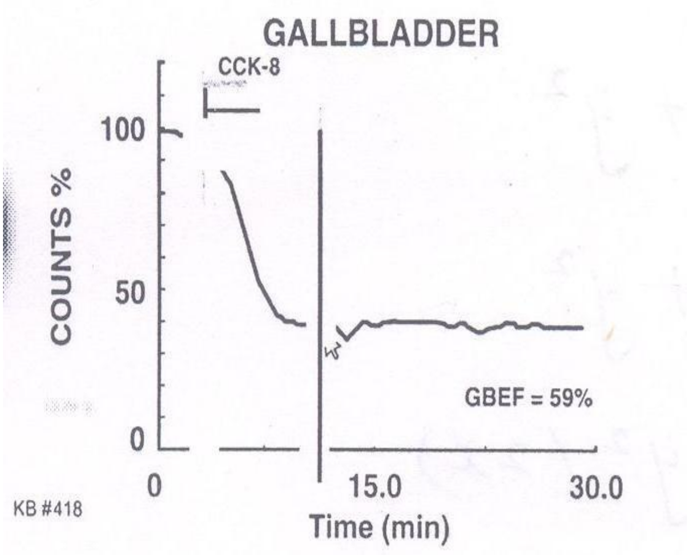
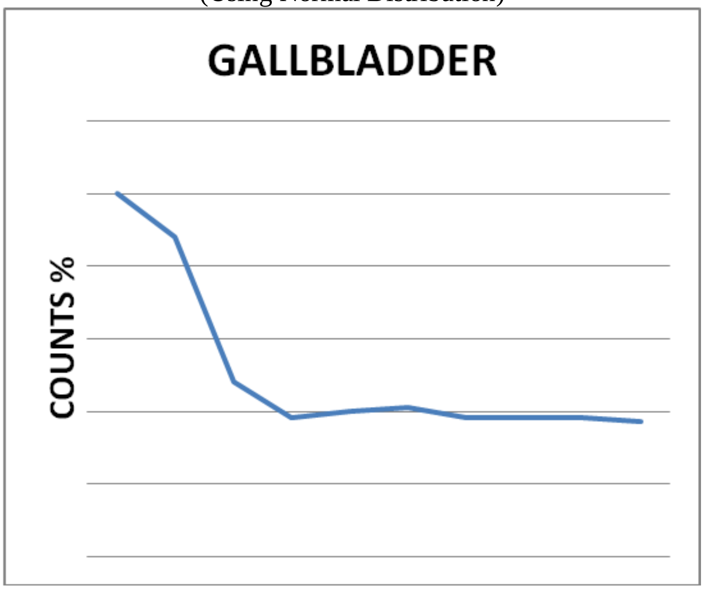


Figure 2: In a normal subject, the gallbladder empties with an ejection fraction of 59% (Using Normal Distribution)



6. Conclusion:

3 minute infusion of 10ng/kg of CCK-8 and a cut off value of 35% as the lower limit of GBEF carries a sensitivity of 95%, specificity of 89% with an overall accuracy of 92% in the evaluation of patients with chronic acalculous choleystitis (CAC). Excellent therapeutic outcome was achieved in CAC patients with laparoscopic cholecystectomy, performed solely on the basis of low ejection fraction; gallbladder ejection fraction with three minute intravenous infusion of 10ng/kg CCK-8 carries both high sensitivity and specificity and clearly separates normal gallbladder from those patients with CAC. The test is simple and reliable. This model is fairly fitted with the non linear diffusion equation by using normal distribution. The medical report {Figure (1)} is beautifully fitted with the mathematical model {Figure (2)}; (i.e) the results coincide with the mathematical and medical report.

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