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Diseases

Infestation of Nematodes

The Etiology of Depression

Highlights

Annandale and Brunetti

The Therapeutic Implications

Discovering Thoughts, Inventing Future

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Infestation of Nematodes in Phlebotomus Argentipes Annandale and Brunetti (Diptera: Psycodidae), Bihar, India

By D.S.Dinesh, V.Kumar & P.Das
Rajendra Memorial Research Institute of Medical Sciences, India

Abstract- Visceral Leishmaniasis (VL) is a major health problem in Bihar, India. The disease is caused by a protozoan parasite Leishmania donovani and transmitted by the established vector Phlebotomus argentipes (Diptera: Psychodidae) in India. P. argentipes transmits viral and bacterial pathogens. Nematodes were isolated from the body of P. argentpes for the first time in India. Its role as pathogen is yet to be established.

Keywords: visceral leishmaniasis, phlebotomus argen-tipes, nematodes.

GJMR-F Classification : NLMC Code: WC 850

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Infestation of Nematodes in Phlebotomus Argentipes Annandale and Brunetti (Diptera: Psycodidae), Bihar, India

D.S.Dinesh [α], V.Kumar [σ] & P.Das [ρ]

Abstract- **Visceral Leishmaniasis (VL) is a major health problem in Bihar, India. The disease is caused by a protozoan parasite Leishmania donovani and transmitted by the established vector Phlebotomus argentipes (Diptera: Psychodidae) in India. P. argentipes transmits viral and bacterial pathogens. Nematodes were isolated from the body of P. argentpes for the first time in India. Its role as pathogen is yet to be established.**

Keywords: visceral leishmaniasis, phlebotomus argentipes, nematodes.

I. Introduction

Visceral Leishmaniasis (VL) is a vector borne parasitic disease caused by a protozoan parasite leishmania donovani and transmitted by the established vector Phlebotomus argentipes Annandale and Brunneti (Diptera : psychodidae) in Bihar, India. P. argentipes also transmits virus and bacteria to the human beings. The transmission of Nematodes is not known so far. The Nematodes or roundworms (Phylum: Nematoda) are the most diverse pseudocoelomates. There are more than 28,000 species of Nematodes (Hugot et al. 2001), of which over 16,000 are parasitic.Sand flies are the main vector of Leishmaniasis. Out of 700 hundred worldwide popu-lations of sand flies, approximately 70 are respo-nsible for transmission of disease to human (Lane 2009). However, these are carrying some entomopathogens like viruses, bacteria, protozoa, fungi, nematods and mites. Phlebotomine sandflies spend most of their lives in dark habitat with stable temperature and high humidity. Their developmental stages from eggs to pupae are passed in crevices, tree buttresses, caves rodent burrows with organic debries like leaf litter and dungs (Killick-Kendrik 1979, 1987). Even adult also prefer the dark and humid diurnal resting sites. These circumstances might be conducive to the development of entomopathogens in sandflies.

It is difficult to find out immature stages of sandflies in nature (Killick-Kendrick 1987), hence, natural pathogens in immature stages in sand flies have not been reported so far. Most of the pathogens were identified from adult sand flies while doing the research work on leishmaniasis (Young and Lewis 1977, 1980). This study reveals the presence of nematodes inside the body of P. argentipes in nature.

II. Material and Methods

Sandflies were collected early in the morning from indoor habitats of dwellings using aspirator and flash light as well as CDC (Centre for Disease Control) light trap. The dissection of gravid females was made in normal saline under dissecting binocular microscopes (Zeiss) and observation was made in high magnification.

III. Results

In the present study 25% P. argentipes were found infested with Nematodes in Bihar, India out of 100 dissected wild populations for the first time collected from villages of Muzaffarpur districts (Figure).

IV. Discussion

Particular work on pathogens of phlebotomines has been conducted by (Killick-Kendrick et al. 1989; Warburg 1991). Many pathogens were found transmitting the diseases. The transmission of phlebovirus, family Bunyaviridae was found infecting mammals (Tesh 1988). The bacterial pathogen like Bartonella bacilliformis, the causative agent of human diseases in some Andean regions of Peru, Ecuador and Colombia is transmitted by Lutzomyia spp. as a group of protozoan kinetoplastids apart from leishmania spp species of Endotrypanum and Trypanosomes are also transmitted by sandflies to vertebrates other than man (Killick-Kendrick 1979; Shaw 1981). In New World Plasmodium spp. the causative agent of reptilian malaria are transmitted by sandflies (Ayala1977; Klein et al. 1988). Entomophtoralean fungi may constitute important pathogens of adult sand flies L. pia in Colombia (Warbug 1991). Saprophytic fungi are found in adult sand flies (Warburg1991) which may influence the development of Leishmania infections (Schlein et al. 1985). Mites (Acarina) collected from sandflies comprise 21 species reported to affecting some 39 species of sand flies hosts. In India mites were found from the body surface of P. argentipes and in laboratory predating the larvae (unpublished).

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Nematodes were reported from different countries in sandflies. Encapsulated third stage spirurid nematodes (rodent infecting Mastophorus muris) have been reported in P. arisasi (Killick Kendrick et al. 1976). Sand fly parasitic nematode i.e tetradonematid was found in P. papatasi and P. sergenti in Afganistan. In adults the nematode interfered with blood feeding by female sandflies(Killick Kendrick et al. 1989). Tylenchid nematodes have been recorded in L. sangunaria, L. vespertilionis and L. panamensis (Mc Conell and Correa 1964) and L. shanoni (Warburg 1991). Eggs, free juveniles and gravid females were recorded in P. papatasi and P. sergenti in Syria by R. Killick-Kendrick was previously in Bagdad (Alder and Theodor 1929). Gregarines(Ascogregarina saraviae) and nematodes (Tylenchida and Spiruda) were recorded in Lutzomyia spp. (Warburg et al. 1991). Infestation of a nematode parasite was observed in the natural population of P. papatasi in Pondicherry, India. Of the 877 males and 959 females sandflies examined for the natural infection, 11 females were found infested with nematodes (0.59%). The presence of a stylet at the opening of the dorsal oesophageal duct suggests that the parasite belongs to the super family Tylenchoidea (Srinivasan et al. 1992). It requires detail studies on sand flies to find out any role of P. argentipes in transmission of helminthes diseases in human in India.

V. Acknowledgements

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Caption:

Figure : Nematodes collected from sandflies after dissection

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Urinary Excretion and Renal Clearance of Allopurinol in Male Gout Patients

By Bilal Ahmed, Tahira Iqbal, Farah Latif & Imtiaz Sohail
University of Agriculture Faisalabad, Pakistan

Abstract- Drugs removed from the body either without changing from its original form or in the form of its metabolite. Allopurinol drug decreases uric acid level in blood and it is used for the treatment of gout and tumor lysis syndrome. Allopurinol and its active metabolite oxipurinol stop the function of xanthine oxidase which forms uric acid from xanthine and hypoxanthine. In this study a quantitative assay using high-performance liquid chromatography (HPLC) with UV-detection was used as a method for quantification of allopurinol and oxipurinol in human serum and urine samples of gout patients after allopurinol administration. The urinary excretion and renal clearance was determined in male gout patients. Blood and urine samples of the human male patients of gout (n=10) after the oral administration of 300mg drug were taken at different time intervals. Results of this study show that there is slow metabolism of allopurinol inside body due to its extensive bonding with blood proteins. Statistical analysis was performed by expressing all the data as mean and ± standard error of mean. The effect of pH and diuresis on renal clearance of allopurinol was studied by regression analysis.

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Bilal Ahmed [α], Tahira Iqbal [σ], Farah Latif [ρ] & Imtiaz Sohail [ω]

Abstract- Drugs removed from the body either without changing from its original form or in the form of its metabolite. Allopurinol drug decreases uric acid level in blood and it is used for the treatment of gout and tumor lysis syndrome. Allopurinol and its active metabolite oxipurinol stop the function of xanthine oxidase which forms uric acid from xanthine and hypoxanthine. In this study a quantitative assay using high-performance liquid chromatography (HPLC) with UV-detection was used as a method for quantification of allopurinol and oxipurinol in human serum and urine samples of gout patients after allopurinol administration. The urinary excretion and renal clearance was determined in male gout patients. Blood and urine samples of the human male patients of gout (n=10) after the oral administration of 300mg drug were taken at different time intervals. Results of this study show that there is slow metabolism of allopurinol inside body due to its extensive bonding with blood proteins. Statistical analysis was performed by expressing all the data as mean and ± standard error of mean. The effect of pH and diuresis on renal clearance of allopurinol was studied by regression analysis.

I. Introduction

Excretion is a process by which drug is removed from the site of action and eliminate from the body. The body begins to eliminate the drug by hepatic or renal metabolism or in some cases both, after administration of dose. The renal clearance of a substance is the volume of plasma that is completely cleared of a substance by the kidney per unit time. The kidneys are the primary mean for elimination waste products of metabolism that are no longer needed by the body. These products include urea, creatinine, uric acid and end product of hemoglobin breakdown and hormone metabolites. These waste products must be eliminated from the body as rapidly as they produced. The kidneys also eliminate most toxins and other foreign substances that are either produced by the body or ingested, such as pesticides, drugs and food additives. The two kidneys lie on the posterior wall of abdomen, outside the peritoneal cavity. Each kidney of adult human weights about 150 grams and is about in size of clenched fist. The medial side of each kidney contains an indented region called the helium through which pass the renal artery and vein, lymphatic's, nerve supply and ureter which carries the final urine from the kidney to the bladder, where it is stored until emptied (Guyton and Hall, 2000).

Renal clearance is quantity of fluid which is filtered out from blood through kidney or 'quantity of blood cleared in unit time' (Seldin, 2004). Allopurinol is structural analogue of xanthine oxidase which is enzyme for uric acid production. The active metabolite of allopurinol is oxipurinol which inhibit the xanthine oxidase. Xanthine oxidase converts xanthine and hypoxanthine into uric acid which increases from its limit and causes gout in humans. Allopurinol is taken through injection or in the form of tablet. If allopurinol is taken orally then after 1hour it achives high serum concentration and its bioavailability is about 67 to 90% withen this time period (Mathus et al, 2007). Allopurinol first convert into oxipurinol by the enzyme aldehyde oxidase and oxipurinol is metabolic product of allopurinol. In urine allopurinol remains unchanged about 10% of its total and about 70% is converted in the form of its metabolite oxipurinol form remaning 20% is excreted through feaces (Hande et al, 1984). The patients of renal disfunction should receive low concentration of allopurinol because increased oxipurinol concentration in plasma is very toxic for this type of patients (Perez et al, 2005). In case of renal impairment the allopurinol dose adjustment should be done by analyzing the creatinine clearance of that patient or it can be optimized by observing the serum concentration level of oxipurinol (Takada et al, 2005). Active metabolic product of allopurinol (oxipurinol) and allopurinol itself are the inhibitors of the enzyme xanthine oxidase which main function is the conversion of hypoxanthine into the xanthine and then xanthine into uric acid. Allopurinol mainly use in the management of long-lasting gout and the condition of hyperuricaemia linked with leukaemia. Allopurinol is a purine base isomer of significance as an anti gout agent. (Rodolfo and Juvencio 2003). Through the process of excretion allopurinol eliminated from the body and removed mostly through urine within certain time period. All metabolic products of allopurinol are removed through excretion. The kidney is a main organ for excretion of allopurinol in almost all mammals (Namazi, 2004). The purine base heterocyclic family of drugs and their basic equivalents are related in pharmacologic and biochemical procedures. From these heterocyclic allopurinol (pyrazolo[3,4-d] pyrimidinic-6one) (ALP), which is anti hyperuricemic drug efficiently guard the

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heart alongside harm due to free oxygen base radicals (ROS) on patients suffering heart bypass operation. But however the mechanism behind this protection is yet not well known. Allopurinol is a anti oxidizing drug that inhibit the xanthine oxidase enzyme necessary for uric acid synthesizing inside the body (Veller et al. 1994). The xanthine oxidase produces reactive oxidizing species in ischemic situation inside body which causes hyperuresemia and raises uric acid level and cause gout however a direct hunting ability of allopurinol and its metabolite oxipurinol alongside extremely oversensitive per oxidants as hydroxide free radical and hypochlorous acid radical. Allopurinol has showing to apply an inhibitory action counter to copper mediated ascorbic acid and DNA oxidation (Domenico et al. 1998). The allopurinol producing companies clearly demonstrate that therapeutic range of oxipuranol in human serum must be 5-15 mg/liter (Hande et al, 1998). If allopurinol and uricosauric drugs are coadministered then oxipuranol renal clearance increases. These drugs used for decreasing serum urate level by interaction with (URAT1) transporter (Iwanageer et al, 2005). The uricosauric drugs combination with allopurinol is only done in the condition of severe gout patients but whatever a condition the serum oxipurinol level should be optimized. The patient use allopurinol monitored by therapeutic drug monotring for verification of patient adherence for proper handling of complications (Stamp et al, 2000). Allopurinol lowers the uridine and uric acid concentrations in plasma and the urinary elimination of uric acid but increased oxypurines and orotidine plasma concentration while urinary excretion of benzbromarone lowers the concentration of uric acid in plasma and increased the excretion of uric acid in urine. However it did not altered the plasma level of uridine or oxypurines or the urinary excretion of oxypurines or orotidine (Tetsuya et al. 1997). Serum uric acid level is typically increased in gout patients. The recommended serum uric acid level must be lowered to a range of < 6 mg/dL for the management of gout symptoms and to decreased acute gout risks (Shoji et al, 2004). Uric acid is excreted through kidney however if kidney function is impaired hyperuricemia may occurred this can also happens in the individuals with normal renal function. If there is a hyperuricemia it may be correlated with incidence of renal impairment and raised the healthcare operation and expenses (Avram and Krishnan, 2008). In case of chronic kidney disease treatment of gout is complicated due to the full treatment by allopurinol. The renal impaired patients had recommended that they should take reduced amounts of allopurinol as they may be at risk for allopurinol toxicity (Hande et al, 1984). Allopurinol is a uric acid lowering drug used in the treatment of gout and the prevention of tumor lysis syndrome. Therapeutic drug monitoring is an important option for evaluation and optimization of allopurinol treatment in case of renal impairment interaction with uricosauric drugs or to verify patient adherence (Mattheus et al. 2007).

Material and Methods. This study was conducted to analyze the urinary excretion and renal clearance of allopurinol and endogenous creatinine in blood and urine. Samples of male gout patients after the oral administration of 300 mg allopurinol were collected. The experiments were conducted on 10 male gout patients. The gout patients who offered to participate was included in this study. The complete demographic data including the age body weight' height, blood pressure and body temperature of gout patients were recoded and presented in Tablet 3.1. Blank blood and urine samples were taken from each gout patients.

Table 3.1 : Demographic data of male gout patients.

Gout patients	Age (Years)	Body Weight (kg)	Height (Ft)	Body Temperature ˚F	Blood pressure (mm Hg)	
					Systolic	Diastolic
1	33	60	5.8	98.2	80	120
2	36	69	5.9	98	70	110
3	39	72	5.7	98.1	80	110
4	35	78	5.6	98	80	120
5	32	74	5.9	98	70	110
6	43	68	5.9	97	80	120
7	45	73	5.8	98.1	70	115
8	42	77	5.9	97.5	80	120
9	49	67	5.7	98	80	160
10	44	76	5.6	98	70	130
Mean ±	38	75	5.8	97.8	76	120
SEM	2.7	6.3	0.16	0.3	4.8	6.5
Minimum	32	60	5.6	97	70	110
Maximum	49	78	5.9	98.2	80	160

II. Sampling Procedure

a) Collection of blood samples

The blood samples of each gout patients were collected after 1 and 3 hours of post medication. After the oral intake of allopurinol 300mg (Zyloric) then take serum from these blood samples and stored in ependorf tubes at -20˚C until use for the analysis.

b) Collection of urine samples

Urine samples of gout patients were collected after 2, 4, 6, 8, 12 and 24 hours after drug administration. These urine samples were stored in plastic bottles in freezer at -20˚C until analysis.

III. HPLC Analysis

Concentration of allopurinol was determined by HPLC.

IV. Chromatographic System

Chromatography was performed with a high performance liquid chromatography. The HPLC system was consisted of Shimadzu SCL-10A system controller, UV visible SPD-10AV detector and LC-10AT pump with FUC-10AL VP flow controller wall. Separation was achieved at ambient temperature with Hypersil C18 BDS 250x4.6 column pore size of 5 micron. Chromatographic data was collected and analyzed using CSW32 software.

V. Chromatographic Conditions

Quantitative analysis of allopurinol was achieved by using an isocratic mode. UV detector was use for the detection of allopurinol. Hypercil C18 BDS 250*4.6 column was used. Flow rate was maintain at 1ml/min with 20 min run time.

Table 3.2 : Concentration and peak area of standard solution of allopurinol in serum

Sr. No.	Concentration (µg/ml)	Peak Area (mv)
1	10	3.3
2	20	8.7
3	30	11.2
4	40	15.4
5	50	25.2
6	300	120.5

a) Preparation of mobile phase

The mobile phase was prepared by dissolving 2.72 g NaCH3COO·3H2O in 3000mL distilled water and correcting the pH to 4.5 with acetic acid 30%. The mobile phase was filtered and degassed before use. The mobile phase was filtered in vacuum filtration assembly having cellulose filter which have pore size 0. 45um (Sartorius company). Filterd mobile phase was solicited for the removal of bubbles for 10 minutes. (eyela sonicator)

VI. Standards Preparation

Stock solution Stock standard solution of allopurinol (0.25 mg/mL) was prepared in deionized water. Stock solution was stored for further analysis.

a) Preparation of working standards in serum

Drug free serum was taken firstly and added working standard of allopurinol of specific concentration 10, 20, 30, 40, 50 and 300µg/ml and mix it with 10% per chloric acid solution (50µL). After cooling in the refrigerator for 10 min dichloromethane (200µL) was added. After shaking the mixture for 30 s, it was centrifuged at 4000 rpm for 5 min. The aqueous supernatant solution was taken. Supernatant was filtered with micro syringe filtration assembly and injected (20µl) into the HPLC instrument for the standard curve. Peak area (mv) versus serum concentration µg/mL of standard allopurinol was plotted and a linear relationship was obtained. This is given in Table 3.2.

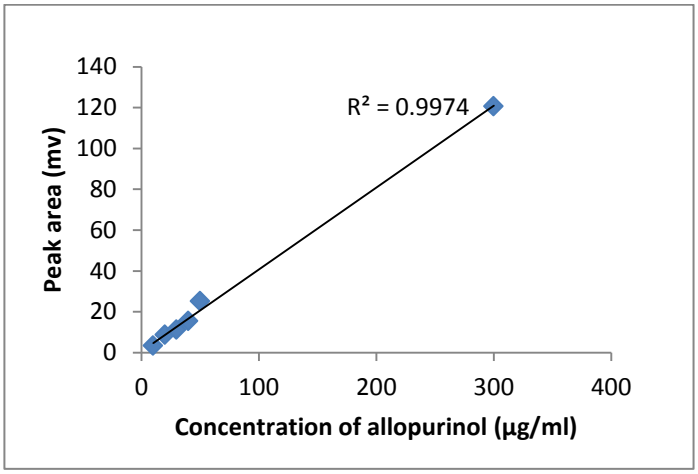


Figure 3.1 : Standard curve of allopurinol in serum.

Preparation of working standards in urine. Drug free urine was taken firstly and added working standard of allopurinol of specific concentration 10, 20, 30, 40, 50 and 300µg/ml and mix it with 10% per chloric acid solution (50µL). After cooling in the refrigerator for 10 min dichloromethane (200µL) was added. After shaking the mixture for 30 s, it was centrifuged at 4000 rpm for 5 min. The aqueous supernatant solution was taken. Filter and a linear relationship was obtained. The data related to standard concentration of allopurinol in urine were presented in Table

Table : Concentration and peak area of standard solution of allopurinol in urine

Sr. No	Concentration (µg/ml)	Peak area(mv)
1	10	7.5
2	20	10.7
3	30	13.3
4	40	29.1
5	50	32.7
6	300	153.25

VII. Calculations

a) Diuresis

The rate of urine flow in a time period was calculated as Volume of urine in a collection time period

$$\text{Diuresis mL/min/kg} = \frac{\text{Volume of urine in a collection time period}}{\text{Time (min) x body weight (kg)}}$$

VIII. Renal Clearance

Renal clearance was calculated by the following formula.

$$\text{Renal clearance (Cl)} = \frac{Uc \times D}{Pc}$$

Uc = Concentration of a drug in Urine
D = Diuresis
Pc = Concentration of a drug in serum

IX. Clearance Ratio

It is calculated by dividing renal clearance of drug by creatinine renal clearance Renal clearance of drug (Cld)

$$\text{Clearance Ratio} = \frac{\text{Renal clearance of drug (Cld)}}{\text{Renal clearance of creatinine (ClCr)}}$$

this supernatant with micro syringe filtration assembly then injected (20µl) into the HPLC instrument for the standard curve. Peak area (mv) versus urine concentration µg/mL of standard allopurinol was plotted

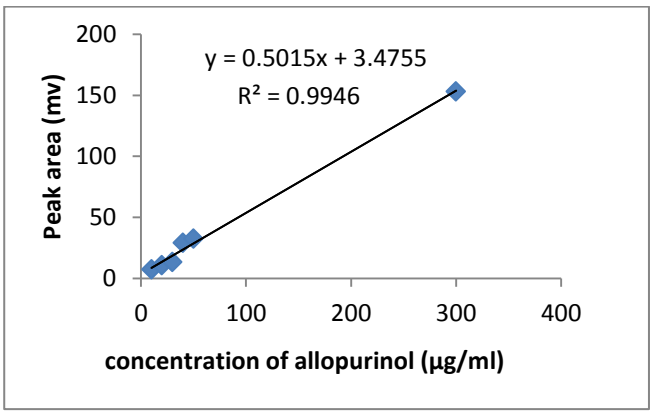


Figure 3.2 : Standard Curve of allopurinol in urin.

X. Urinary Excretion

Amount of Allopurinol (mg) excreted in urine at different time intervals were calculated by using formula:

$$\text{Amount excreted (mg)} = \frac{\text{Concentration of drug (µg/mL) x urine volume}}{1000}$$

Percentage dose of allopurinol excreted in urine at different time intervals was calculated by formula:

$$\text{Percentage dose (\%)} = \frac{\text{Amount excreted (mg)}}{\text{Amount of dose (mg)}} \times 100$$

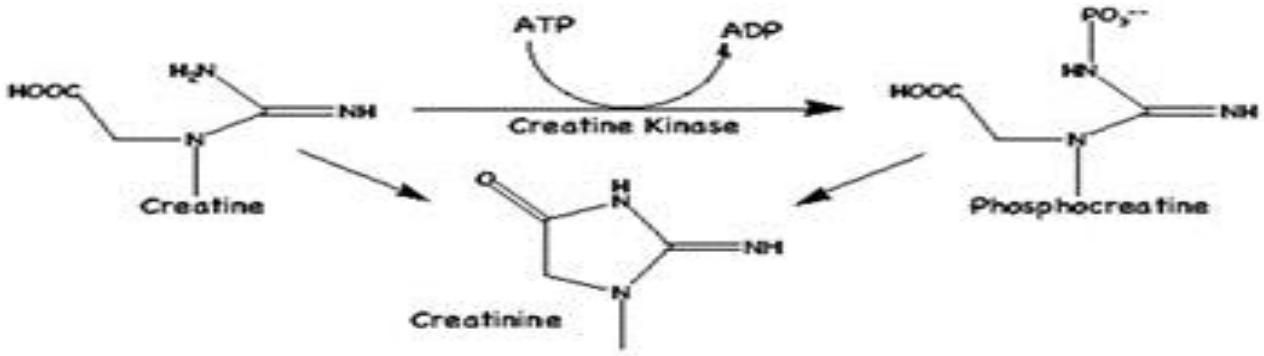
$$\text{Cumulative percentage dose excreted} = \frac{\text{Cumulative amount excreted}}{\text{Amount of dose (mg)}} \times 100$$

XI. Determination of Allopurinol in Samples

The procedure for determination of allopurinol in serum and urine sample is similar to that of standard solution.

XII. Creatinine Analysis

Creatinine analysis was performed by creatinine colorimetric detection kit of (merck company). Some important parameters due to which this method was preferred upon conventional method. The Creatinine colorimetric detection kit utilizes a single-step liquid detection reagent that is safer and less time consuming than other assay methods. This kit is calibrated against the NIST standard and offers reproducible results with less than 6% inter- and intra-assay variation.



Creatinine (2-amino-1-methyl-5H-imadazol-4-one) is a metabolite of phosphocreatine (p-creatine), a molecule used as a store for high-energy phosphate that can be utilized by tissues for the production of ATP. Creatine either comes from the diet or is synthesized from the amino acids arginine, glycine, and methionine. This occurs in the kidneys and liver, although other organ systems may be involved and species-specific differences may exist. Creatine and p-creatine are converted non-enzymatically to the metabolite creatinine, which diffuses into the blood and is excreted by the kidneys. In vivo, this conversion appears to be irreversible and in vitro it is favored by higher temperatures and lower pH. Creatinine forms spontaneously from p-creatine, and under normal conditions, its formation occurs at a relatively constant rate. Intra-individual variation of creatinine levels is <15% from day to day, making it a useful marker for normalizing levels of other molecules found in urine. Altered creatinine levels may be associated with conditions that result in decreased renal blood flow, such as diabetes and cardiovascular disease.

XIII. Statical Calculations

The data on renal clearance was tabulated. The statical calculations were done according to the standard method and results are given as average standard error. The correlation between diuresis and serum concentration of drug and renal clearance was determined by mean off regression / correlation analysis (Steel and Torrie, 2001). The results have been presented in table and graph. Graph and table have been presented in Microsoft excel version 2010.

XIV. Results

The urinary excretion and renal clearance of allopurinol was investigated in ten male gout patients after the oral administration of 300 mg tablet. Blood and urine samples were taken at different time intervals post medication and concentration of allopurinol in each sample was determined by HPLC method. The volume of urine, concentration of creatinine and allopurinol in the urine and serum were measured to calculate diuresis, renal clearance of creatinine and drug and clearance ratio. The results of urinary excretion of allopurinol were expressed in terms of amount excreted in mg, percentage dose excreted, cumulative amount excreted and cumulative percentage dose excreted. Concentration (µg/mL) of allopurinol in urine At 2 hours after drug administration Mean ± SEM value of concentration (µg/mL) of allopurinol in urine was 3.818 ±0.326. At 4 hours after drug administration Mean ± SEM value of concentration (µg/mL) of allopurinol in urine was 23.4160± 5.838. At 6 hours after drug administration Mean ± SEM value of concentration (µg/mL) of allopurinol in urine was 17.30 ± 3.61. At 8 hours after drug administration Mean ± SEM value of concentration (µg/mL) of allopurinol in urine was 11.72 ± 3.18. At 12 hours after drug administration Mean ± SEM value of concentration (µg/mL) of allopurinol in urine was 5.77 ± 1.20. At 24 hours after drug administration Mean ± SEM value of concentration (µg/mL) of allopurinol in urine was 4.16 ± 0.60. Peak concentration in urine of allopurinol is achieved within 6 to 8 hours while before and after this the concentration is very low this is due to the reason that the metabolism of allopurinol inside the human body is slow may be due to the extensive bonding ability of allopurinol with the serum proteins.

a) Amount (mg) Excreted

At 2 hours after drug administration ±SEM amount (mg) of allopurinol excreted in urine was 6.1±1.3. At 4 hours after drug administration mean ±SEM amount (mg) of allopurinol excreted in urine was 9.03± 1.56. At 6 hours after drug administration mean ±SEM amount (mg) of allopurinol excreted in urine was 2.8± 0.403. At 8 hours after drug administration mean ±SEM amount (mg) of allopurinol excreted in urine was 3.7± 1.46. At 12 hours after drug administration mean ±SEM amount (mg) of allopurinol excreted in urine was 4.9± 1.36. At 24 hours after drug administration mean ±SEM amount (mg) of allopurinol excreted in urine was 13.24± 2.90

b) Cumulative Amount Excreted

At 2 hours after drug administration mean ±SEM value of cumulative amount of allopurinol excreted in urine was 6.080± 1.10. At 4 hours after drug administration mean ±SEM value of cumulative amount

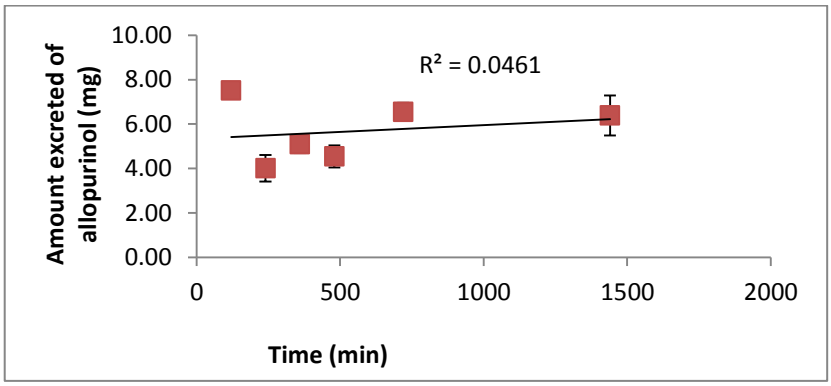


Figure 4.1 : Amount excreted of allopurinol in ten male gout patients after oral administration of allopurinol (300mg).

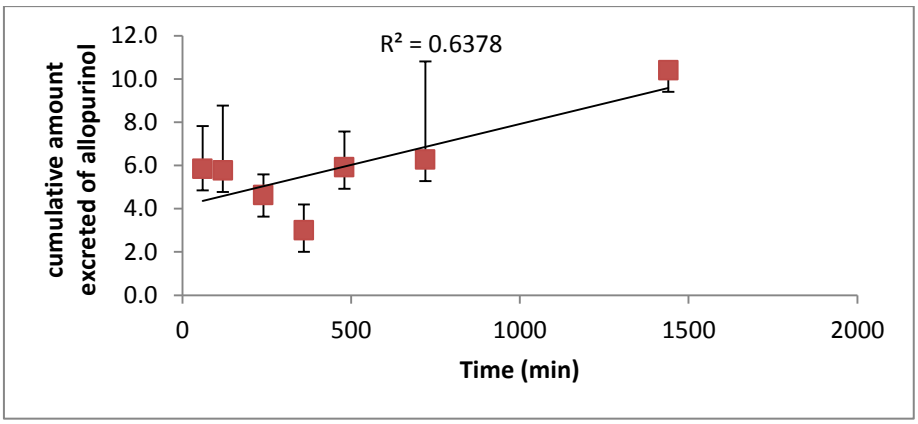


Figure : Cumulative amount of allopurinol excreted in

of allopurinol excreted in urine was 15.11± 2.1. At 6 hours after drug administration mean ±SEM value of cumulative amount of allopurinol excreted in urine was 17.81±2.8. At 8 hours after drug administration mean ±SEM value of cumulative amount of allopurinol excreted in urine was 21.72± 2.4. At 12 hours after drug administration mean ±SEM value of cumulative amount of allopurinol excreted in urine was 26.23± 3.33. At 24 hours after drug administration mean ±SEM value of cumulative amount of allopurinol excreted in urine was 38.57± 4.8.

urine of ten male gout patients at different time intervals after oral administration of (300 mg) allopurinol.

c) *Creatinine Concentration in Serum*

The mean ± SE value of serum concentration of creatinine was 2.91±0.081µg/ml while it varied from 2.40 to 3.30µg/ml.

d) *Creatinine Concentration in Urine*

Creatinine concentration in urine varied from 3.89 to 29.5µg/ml and its mean value is 18.98±3.63µg/ml.

e) *Renal clearance of creatinine*

Mean ±SEM value for renal clearance of endogenous creatinine was 7.16±3.83 ml/min/kg. While it varied from 0.58 to 33.83 ml/min.kg.

f) *Allopurinol clearance*

Renal clearance of allopurinol was determined in ten human male gout patients after oral administration of 300 mg allopurinol tablet. Results are presented.

g) *Allopurinol concentration in serum*

The mean ± SEM value of serum concentration of allopurinol was 55.76±1.91µg/ml while it varied from 46.76 to 64.76µg/ml.

h) *Allopurinol concentration in urine*

Allopurinol concentration in urine varied from 7.34 to 19.36 while its mean ±SE value was 11.039± 1.13µg/mL.

i) *Renal clearance of allopurinol*

The mean ±SEM value of renal clearance of allopurinol calculated was 0.037±0.009 ml/min/kg and it ranged from 0.0004 to 0.0012 ml/min/kg.

Table : Mean data of renal clearance of allopurinol and endogenous creatinine in ten healthy male gout patients after oral administration of allopurinol (100mg)

Gout patients	Creatinine concentration (µg/mL)		Allopurinol concentration(µg/mL)		Renal clearance mL/min/kg		Clearance ratio
	Urine	serum	Urine	serum	creatinine	allopurinol	
1	10.4	3.32	8.93	46.76	0.014	0. 09	0.061
2	29.5	2.88	7.41	48.76	0.05	0. 09	0.015
3	33.5	2.89	7.34	50.76	0.04	0. 05	0.012
4	35.2	2.87	10.42	52.76	0.04	0. 08	0.016
5	26.7	3.17	9.69	54.76	0.03	0. 08	0.021
6	7.01	3.08	10.3	56.76	0.005	0. 04	0.08
7	3.89	2.54	13.54	58.76	0.008	0. 12	0.151
8	11.6	2.49	9.97	60.76	0.10	0. 36	0.035
9	19.7	2.91	13.25	62.76	0.03	0. 11	0.031
10	12.3	3.04	19.35	64.76	0.025	0. 19	0.074
Mean	18.8	2.919	11.09	55.76	0.03	0. 12	0.05
±SEM	3.6	0.06	1.13	1.91	0.009	0. 03	0.014

XV. Discussion

Since the mid-1980s the most frequently used technique in the bio analysis of drugs has been high-performance liquid chromatography (HPLC). HPLC usually exhibits its resolving power at ambient or slightly raised temperatures in the liquid phase with the key requirements being that the analyte has some solubility in the liquid mobile phase and some affinity for the solid stationary phase. It is the relative strength of the analytes affinity for each of these phases that gives the technique its separating capability. Another factor in the emergence of HPLC in pharmaceutical applications has been the types of detectors that may be used generically for wide varieties of drugs and which are compatible with HPLC. The most obvious example is the ultra-violet (UV) absorption detector which has found extremely wide use as most drugs have a chromophore which will absorb UV light of the appropriate wavelength. In HPLC separation occurs due to partitioning between a stationary phase contained in a column and a liquid phase which is pumped under pressure through this column (David N. M., 2004). The principle rout of the drug excretion is the urine. Our kidneys produce urine which contains urea, excess salts, drug metabolites and excess water. Kidneys perform two grand functions. First is to get rid of waste materials and second is to control the composition of the body fluids and the body volume. For water and all electrolytes in the body, balance between output (due to excretion or metabolic consumption) and intake (due to ingestion or metabolic production) is maintained largely by kidneys. The kidneys perform their important function by filtering plasma and removing substances from filtrated at variables rates, depending on the needs of the body itself. Ultimately kidneys clear the wasteful materials from the filtrate by excreting them in the urine while returning substances that are needed by the body back to the blood. Kidneys also eliminate most toxic material and other foreign substances that are either produced by the body or ingested, such as pesticides, drugs and food additives. Renal excretion accounts for most drug

elimination that are predominately ionized at physiological pH and for polar drugs, drug metabolites with low lipid solubility. Renal drug excretion decreases with aging. Drugs bound to plasma proteins remain in the circulation; only unbound drug is contained in the glomerular filtrate. Un-ionized forms of drugs and their metabolites tend to be reabsorbed readily from tubular fluids (Guyton and Hall, 2000).Urine pH has a great influence on whether a drug is excreted readily or slowly and in some clinical situations urine pH is maintained to control the excretion of certain drugs from the body. Urine pH plays an important role in the ionization of the drug and its absorption from the tubules. Most of the drugs are either weak acids or weak bases. Acidic drugs are more readily ionized in alkaline urine and alkaline drugs are more readily ionized in acidic urine. Ionized or polar substances are more soluble in water so readily dissolve in the body fluids for excretion (Lin et al., 1988). The present study revealed the result non-significant correlation between the pH and urine concentration. It means pH did not affect the urinary excretion of drug. The main functions of kidney are urine formation and water conservation and this is the major channel of water excretion as compared to intestine, skin and lungs (Ganong, 2005). Creatinine is an anhydride end product of creatine metabolism in muscle. The total creatinine in muscle is 10 mg only. The clearance of creatinine is only slightly higher than GFR this metabolite is filtered at the glomerulus but neither secreted nor reabsorbed by the tubules so its clearance gives the GFR. The functional unit of the kidney is nephron 1.2 million nephrons make up each human kidney. The glomerulus is a modified capillary network that delivers an ultra-filtrate of plasma to Bowman's capsule, the most proximal portion of the nephron. These glomeruli collectively produce 120 to 180 liters of ultra-filtrate daily. The volume of the urine excreted (averaging 1.5L/ day or 1mL/ min) represent the sum of two large, directionally opposite processes namely, ultrafiltration of 180L/day and reabsorption of more than 99% of this filtrate by transport process in the renal tubules. Renal blood flow accounts for about 20% of resting cardiac output, yet the kidneys comprise only about 1% of total body weight. This disproportionate allocation of cardiac output is required for the process of ultrafiltration. These processes glomerular filtration, tubular reabsorption and active tubular secretion are involved in the secretion of all metabolites through kidneys (Choi et al., 1993). In ten male gout patients the renal clearance of allopurinol was studied and results have been discussed below. The Mean value of allopurinol renal clearance was 359±9.7 mL/min (Dowling et al., 2001) while another study suggests that the value is 310 ml/min. The mean value of renal clearance of our study was found to be 11.83±0.6.58 mL/min/kg. The difference between these values is due to different temperature and environment. Within 24 hours of oral administration, some 50-70% of the dose mean was excreted in the urine as unchanged drug. Over the dose range of 0.3-30 mg/kg allopurinol, there was no dose-dependent effect on total or renal clearance 10% of a allopurinol dose being excreted unchanged in urine with the major site of elimination which occurs by renal mechanisms. At the glomerulus allopurinol is mainly secreted. The difference in the urinary excretion of allopurinol under local conditions and reported in literature is due to environmental and genetic influences on glomerular filtration rate which significantly affect the fate of drug in the body. These differences have been elucidated by original term geonetics (Jeffrey et al, 1998). Studies on allopurinol suggest that it is extensively secreted from urine even though when given in small amounts. At serum concentrations up to 30-fold the tubular secretion rate of allopurinol gradually increases and higher than those values which are achieved during 300 mg/day typical oral dosing. The retention time for the present study was 9 min for plasma and 10 min for urine. The difference is probably due to storage of urine and plasma samples, environmental conditions and/or temperature. The present percent dose is lower calculated as 66.30±2.18. There is difference between present study value and earlier study value due to difference in environment, temperature but major difference in the values is due to non-fasting gout patients (Konrad et al. 2002).

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P.Vivax Malaria: A Benign Disease with Emerging Complications

By Dr. Vishal Sadatia & Dr. Ritesh Vekariya
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Abstract- *Background:* Malaria is an endemic disease in India. It is a mosquito-borne infectious disease caused by genus Plasmodium. Complications usually occur with P.falciparum, its occurrence has been rarely reported in cases of P. vivax malaria. We observe 107 patients with P.vivax malaria who developed complications in the form of Thrombocytopenia, Acute kidney injury, hyperbillirubinemia & cerebral malaria, a rare presentation in P.vivax malaria.

Objectives: As the burden of P.vivax malaria is progressively increasing in community this study has been carried out to find out various complications in P.vivax malaria which is considered as a benign entity.

Methods: We prospectively enrolled 150 patients hospitalized in C.U.Shah hospital of P.vivax infection on initial microscopy with complications over a two year period. Hematological, biochemical, serological, radiological investigations are performed to identify complications.

Keywords: *P.vivax malaria, complications of P.vivax, thrombocytopenia.*

GJMR-F Classification : *NLMC Code: WJ 100, WC 750*

Strictly as per the compliance and regulations of:

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Dr. Vishal Sadatia [α] & Dr. Ritesh Vekariya[σ]

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Methods: We prospectively enrolled 150 patients hospitalized in C.U.Shah hospital of P.vivax infection on initial microscopy with complications over a two year period. Hematological, biochemical, serological, radiological investigations are performed to identify complications.

Results: As per study, burden of P.vivax(67%) is more in community as compared to P.falciparum(33%). Out of 150 patients of P.vivax malaria, 107 patients were having various complications in the form of Thrombocytopenia (71.33%), Anemia(10%), hyperbillirubinemia(8.67%), Acute renal failure(8%) and cerebral malaria(1.33%) in their respective order. Most common complication is thromb-ocytopenia. Male gender is more prone to develop complicated P.vivax malaria than female with unknown reason.

Conclusion: As per observations, P.vivax malaria is no more benign disease. P.vivax can be presented with various complications and as far as thrombocytopenia is concern, it has a favorable prognosis and does not require platelet transfusion regularly except sequel is present.

Keywords: P.vivax malaria, complications of P.vivax, thrombocytopenia.

I. Introduction

Malaria is a mosquito-borne parasitic disease. In India it is mainly caused by P.vivax and P.falciparum. Complicated malaria charact-erized by serious organ failures or abnormalities in the patient's blood or metabolism,usually occurs in P.falci-parum malaria. Manifestations of severe malaria include cerebral malaria, severe anemia, hemoglobinuria, AR-DS, thrombocytopenia, cardiova- scular collapse and shock, acute kidney injury, metabolic acidosis and hypoglycemia.

In contrast to falciparum malaria, vivax malaria is rarely associated with serious complication. Scattered cases of P.vivax causing severe malaria have been reported in the last 30 years.

Manifestations of malaria vary from asymptomatic infection to severe malaria. The essential pathologic feature of severe malaria is sequestration of erythrocytes, which contain mature forms of the parasite in the deep vascular beds of vital organs and rosette formation, thus producing organ dysfunction.

P.vivax may no longer be a paradigm for uncomplicated malaria. Presence of thrombocytopenia in acute febrile travelers returning from tropical areas has become highly sensitive marker for malaria diagnosis (D'Acremont et al.2002).The sensitivity of thrombocytopenia together with the acute febrile illness was 100% for malaria diagnosis, with specificity of 70%, a positive predictive value of 86% & a negative predictive value of 100% (Patel et al 2004).

Since the beginning of the 1970s, there have been reports proposing that malaria associated thrombocytopenia is quite similar in P.vivax and P.falciparum infections (Beale et al 1972). Most of the data were published in late 1990s because of an availability of affordable automated machines capable of performing complete blood count (CBC).

II. Material & Methods

- This is a hospital based study conducted on the patients of the medicine department in C.U.SHAH medical college & hospital, Surendranagar(Gujarat) during July 2010 to July 2012.

a) Inclusion Crieteria

- Patients who came in the outdoor dept. and/or admitted in medicine department with complicated P.vivax malaria.

b) Exclusion Criteria

- Patients who came in OPD and/or admitted in medicine dept. but do not have any type of complication of malaria.
- Patients who are having only P.falciparum malaria or mixed infection of P.vivax & P.falciparum malaria.

c) Diagnosis Of Malaria & Various Complications

- Most of the diagnosis is made with the help of conventional study of thick and thin peripheral blood film.
- Rapid antigen detection test is used and confirmed diagnosis, whenever required.

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- The complications of malaria are diagnosed mainly by various biochemical tests in pathology laboratory[SIEMENCE auto analyzer] and chest x-ray.

III. Observation

- Total number of the P.vivax malarial cases observed within 2 years are 150.Out of them 43 cases are uncomplicated and 107 cases are of complicated P.vivax malaria.
- There are various complications in the form of Thrombocytopenia (71.33%), Anemia (10%), hyperbillirubinemia (8.67%), Acute renal failure (8%) and cerebral malaria (1.33%) in their chronological order have been observed in 107 cases of complicated P.vivax malaria.
- As shown in figure 1, out of 225 cases of malaria 150(66.66%) are of P.vivax and remaining 75(33.34%) of P.falciparum malaria.
- As shown in figure 2, the most common complication amongst all P.vivax malarial cases is THROMBOCYTOPENIA. After that Anemia > Jaundice > AKI > Cerebral malaria in their respective order.
- Thrombocytopenia with its sequel (hematuria, hemoptysis, hemetemesis etc.) is present only in few cases [2] & requires blood / platelet transfusion. Otherwise in all other cases thrombocytopenia remains silent without any sequel. So as such thrombocytopenia without any sequel is not a harmful condition.
- The criteria for diagnosis [3] of the complicated vivax malaria as follow…….
  - Thrombocytopenia - PLT < 150000/cumm
  - Anemia - Hb < 9.0gm/dl (severe anemia Hb < 5.0gm/dl)
  - Jaundice - serum billirubin > 2.5 mg%
  - Cerebral malaria – Glasgow coma scale 9/15
  - Renal failure - creatinine >1.8mg%
- As discussed earlier, the most common form of complication is thrombocytopenia; Figure 3 is showing the different ranges of the thrombocytopenia occur in the malarial infection.
- As shown in figure 4, incidence of complicated P.vivax malaria in male is more than female. As such there is no any relation between gender and P.vivax infection[4].
- Age wise distribution (figure 5) is more amongst the people who are in between age group of 21 – 30 yrs. (38%) [Kocher et al]. Other age group distribution in the patients is uneven.
- Various forms of the parasite life cycle which have been observed in the peripheral blood film examination (figure 6). The TROPHOZOIT form followed by RING form is predominantly seen in the PBF study. The least common form of the parasite is GAMATOCYTE. While most of the time one or more types of the form of parasite are found together in the peripheral blood smear study.

IV. Discussion

- Organ dysfunction is characteristic of P.falciparum malaria & unusual in P.vivax infection. Severe complicated malaria is a well-recognized feature of P.falciparum malaria. Although a few cases with P.vivax have been reported in literature. Any patient infected with P. vivax who exhibits severe malaria is presumed to be suffering from mixed infection[5]. However, that may not be always true. As evident from the present report, P.vivax infection can also present with complications.
- Clinical data indicates that P.vivax can cause both sequestrations related and non-sequestration related complications of severe malaria [4]. The exact pathogenetic mechanism however remains elusive. Sachdev and Mohan [6] studied the clinicolaboratory profile of patients with P.vivax cerebral malaria. Focal neurological signs were observed in one patient. Recently a case of cerebral vivax malaria that presented with status epilepticus has been described [7].
- P.vivax malaria without any complication has been reported many times, even remains silent[8]. It may be presented occasionally with mild anemia or febrile illness. However, none of them had any evidence of thrombocytopenia, AKI and recovered without any sequel[8,9].
- However almost all type of complications have been found in this study, but more common one is thrombocytopenia.
- There are reports of thrombocytopenia occurring as a manifest of P.vivax malaria in adults. The mechanism of thrombocytopenia (figure 9) in malaria is not clearly known….
  1. Decreased thrombopoiesis, although this hypothesis was later ruled out [9,10]
  2. Thrombocytopenia is a result of peripheral destruction in which immune complexes generated by malarial antigens lead to sequestration of the injured platelets by macrophages in the spleen, although this mechanism has not been systematically evaluated in P.vivax malaria[1,11] .
  3. An inverse relationship between elevated parasite levels and decreased platelet counts observation consistently has been reported for P.vivax infection[12].
- Fajardo and Tallent[9] in 1974 demonstrated P.vivax within platelets by electron microscopy and suggested a direct lytic effect of the parasite on the platelets. Both non-immunological destruction[13] as well as immune mechanisms involving specific platelet-associated IgG antibodies that bind directly to the malarial antigen in the platelets has been

recently reported to play a role in the lysis and the development of thrombocytopenia[14].

- Oxidative stress damage of thrombocytes has also been responsible based on the finding of low levels of platelet superoxide-dismutase and glutathione peroxidase activity and high platelet lipid peroxidation level in malaria patients, when compared to those of health subjects[15].
- Malaria may cause anemia and hyperbillirubinemia because of the loss of red blood cells. Intravascular hemolysis & DIC in P.vivax malaria can cause ARF, which occurs more in P.falciparum malaria but we found 8% cases in p.vivax infection[10] . Renal ischemia is the dominant pathogenic mechanism that results in acute tubular necrosis. The prognosis of ARF in P.vivax malaria is favorable.

V. Conclusion

- P.vivax may no longer be a paradigm for uncomplicated malaria. It has been observed that the burden of complicated P.vivax malaria is progressively increasing.
- Complications are common in the form of Thrombocytopenia(71.33%), Anemia (10%), hyperbillirubinemia(8.67%), Acute renal failure(8%) and cerebral malaria(1.33%) in their respective order. As far as the thrombocytopenia is concerned, it is having favorable prognosis & most of them were recovered with only antimalarial treatment so routine use of platelet transfusion is not recommended in a case of thrombocytopenia.
- P.vivax now a days emerging as one of the cause of isolated thrombocytopenia. It is a challenge to differentiate P.vivax from falciparum malaria and Dengue fever.

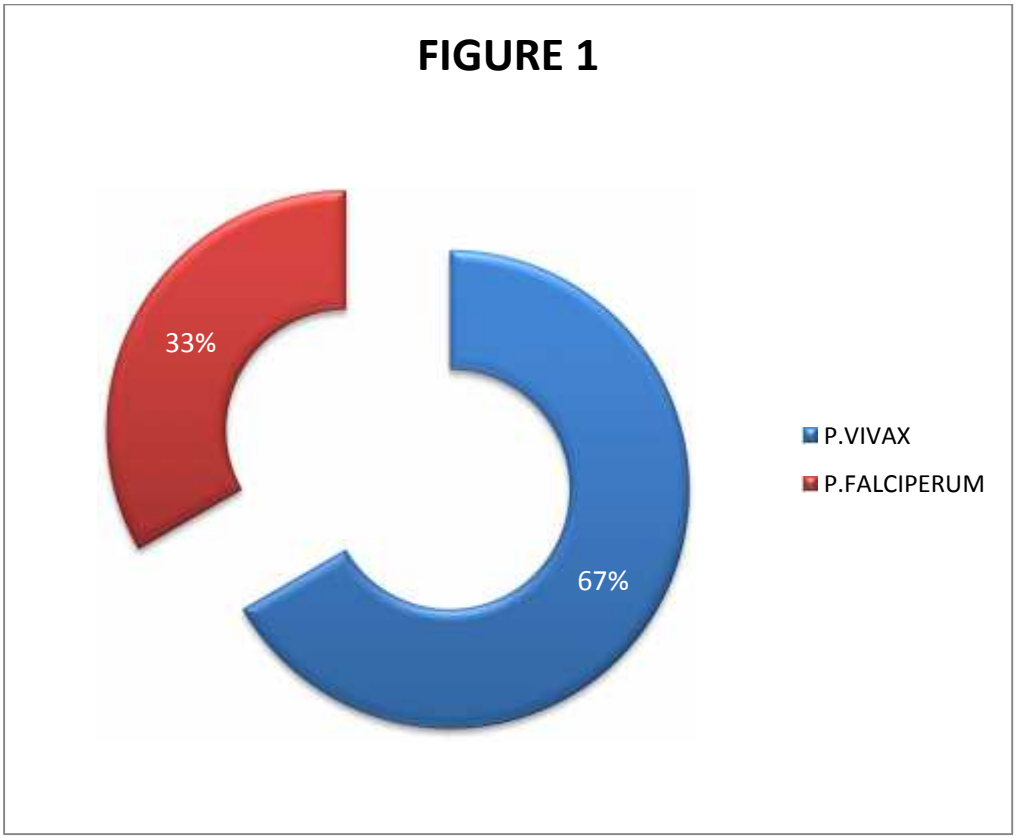

Figure 1 : Incidence of the P.Vivax Malaria

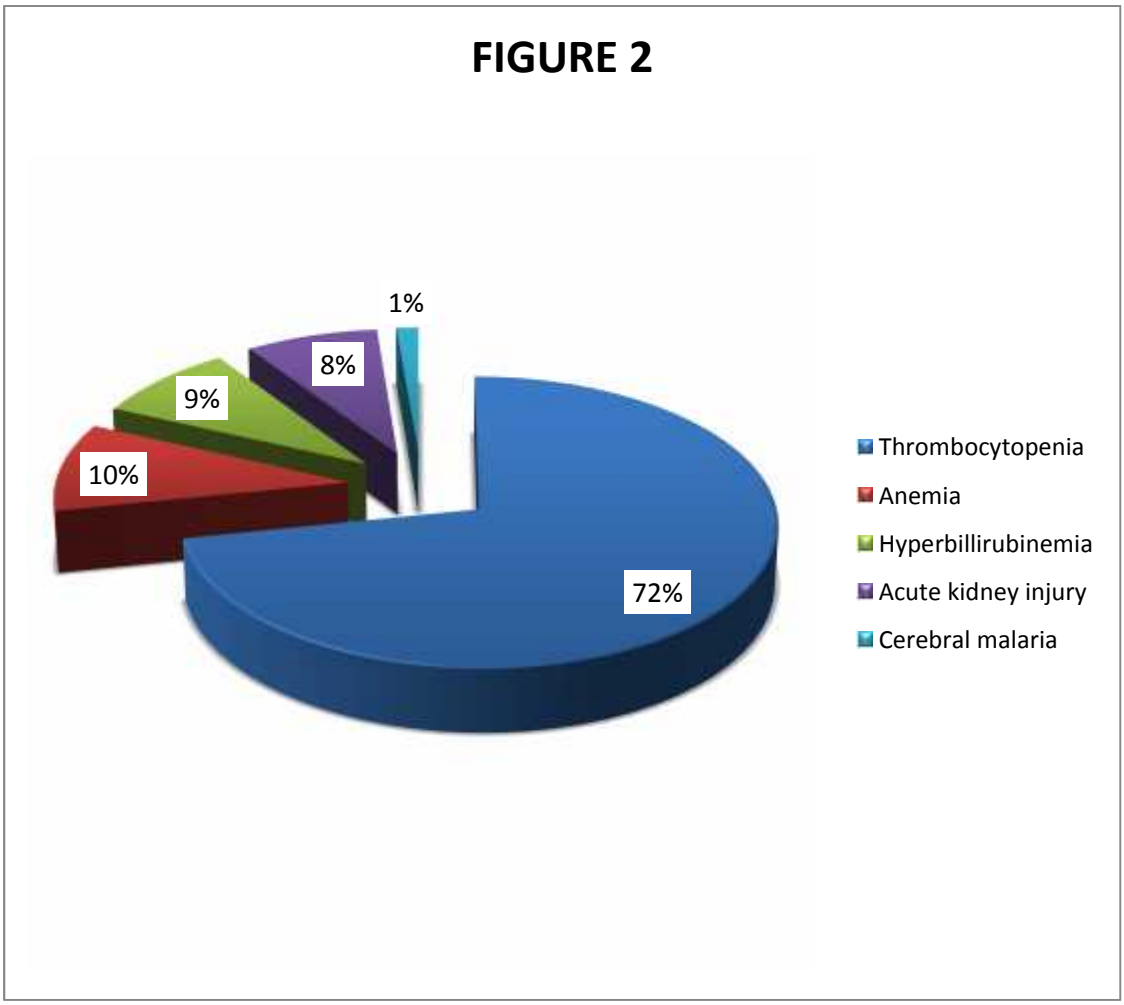

Figure 2 : Incidence of Complications of

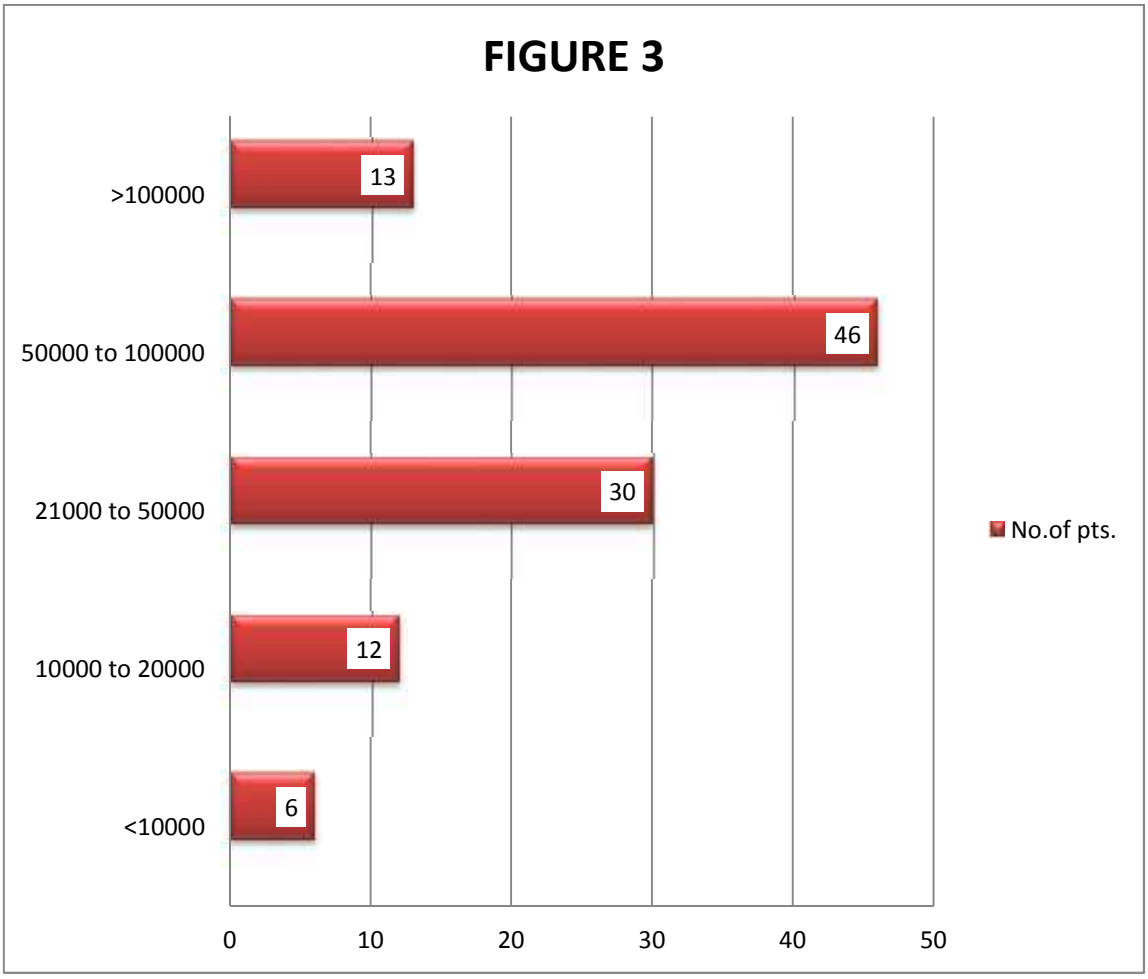

Figure 3 : Incidence Of Severity Of Thrombocytopenia

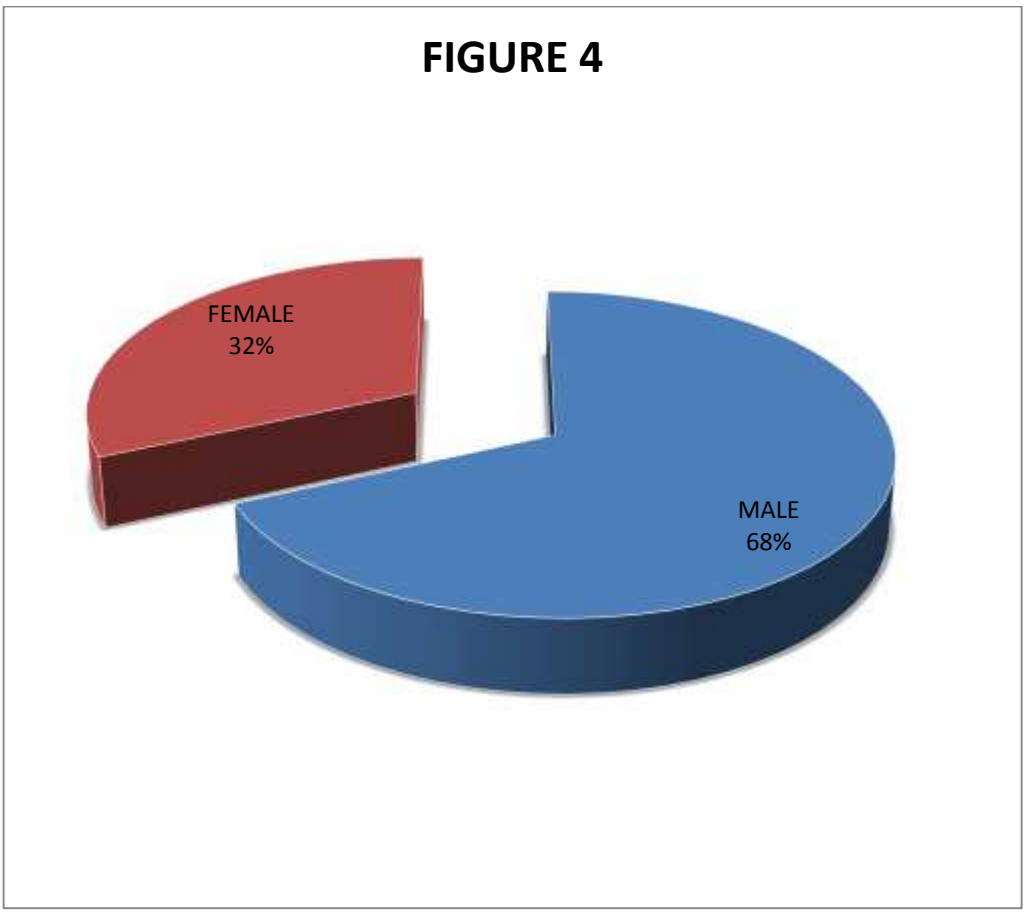

Figure 4 : Incidence Of P.Vivax In Male & Female Gender

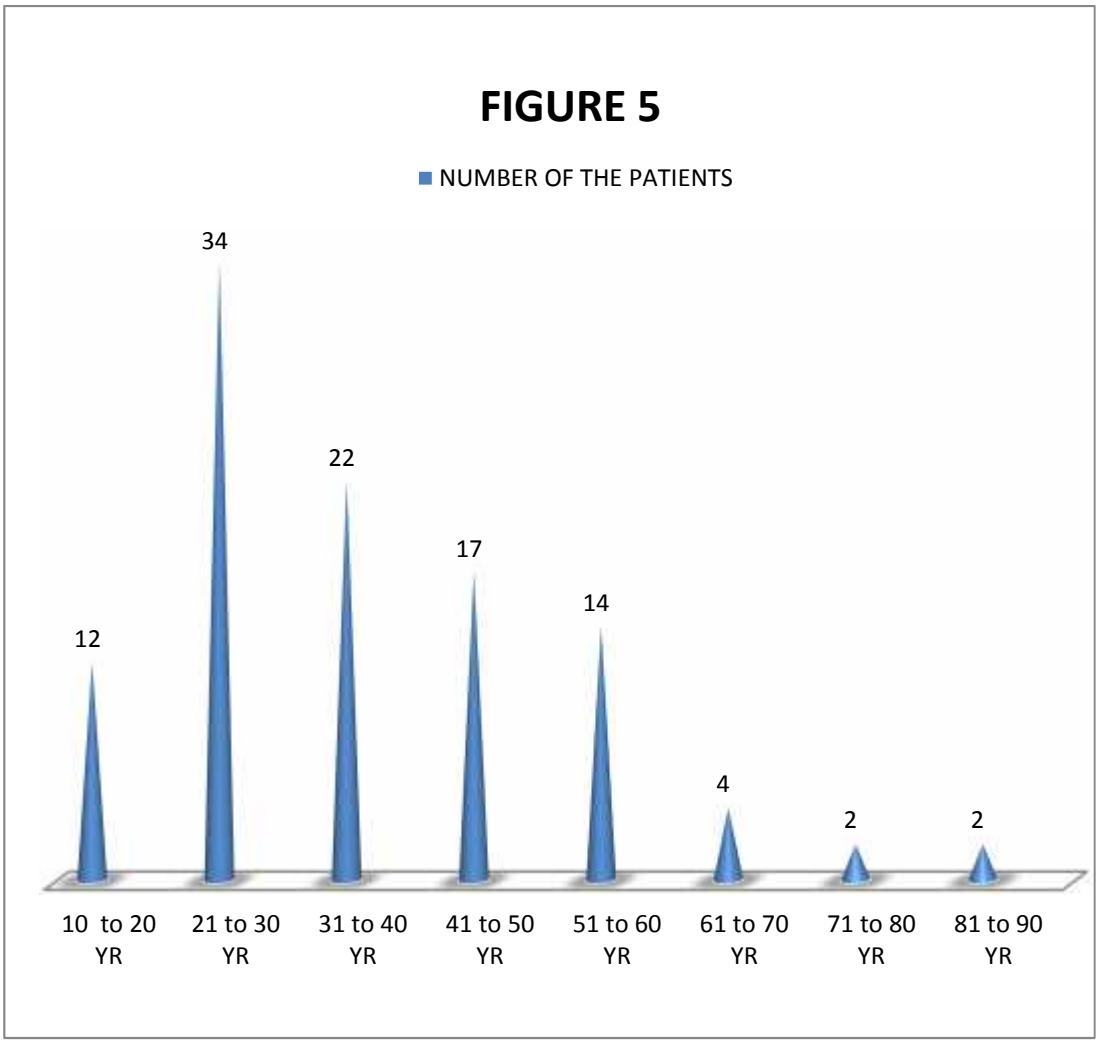

Figure 5 : Age Wise Distribution Of P.Vivax Malaria

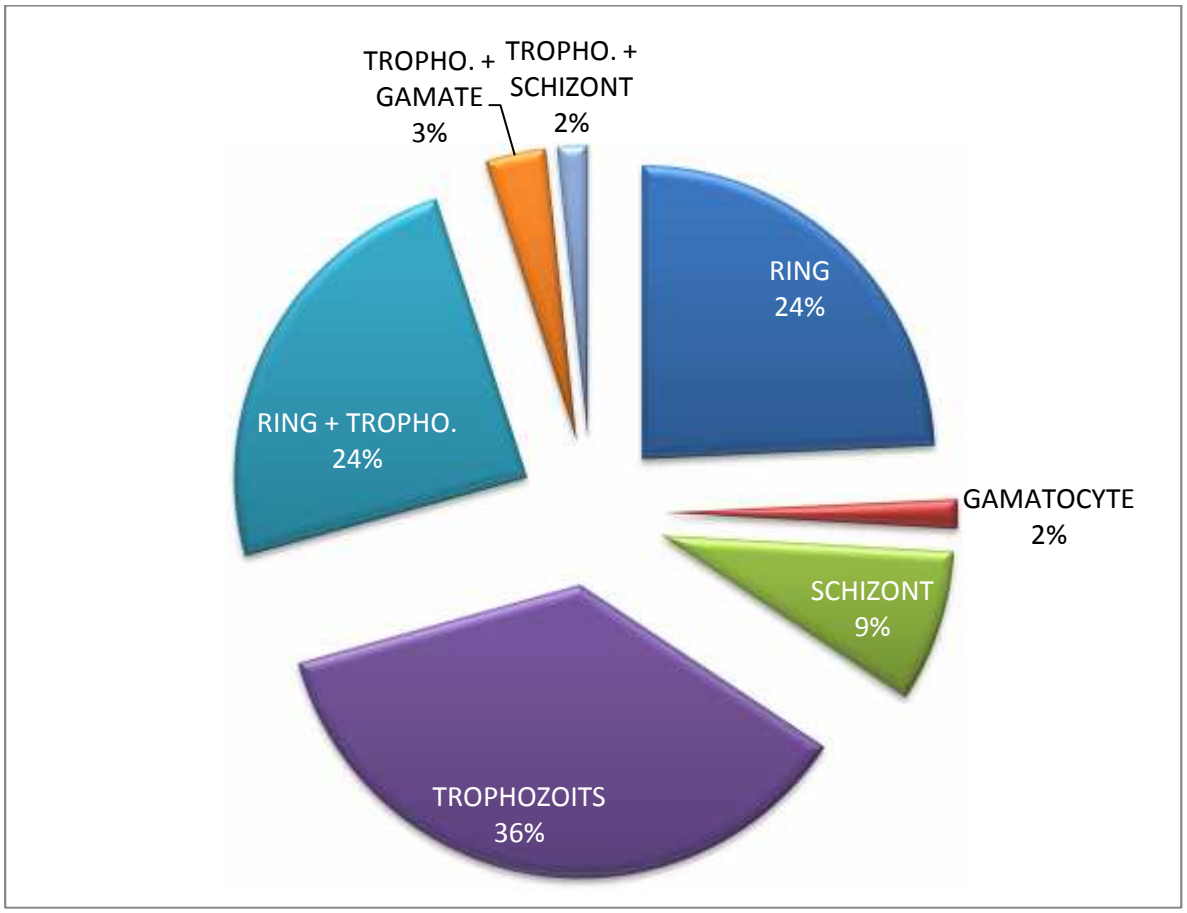

Figure 6 : Various Forms Of Lifecycle Of P.Vivax In Peripheral Blood Film

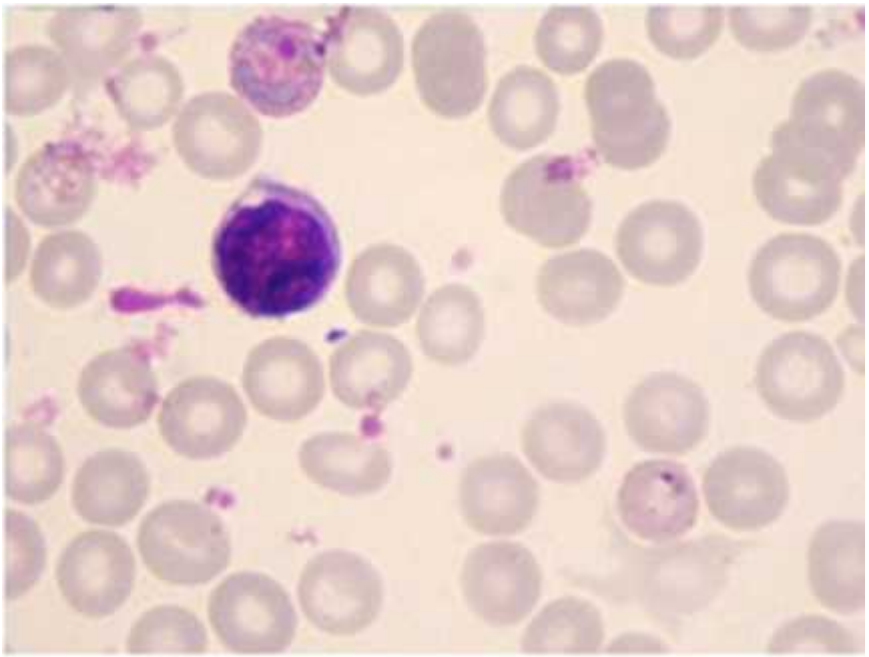

Figure 7 : (Malarial Parasite Found In Rbc On Periferal Blood Smear Study)

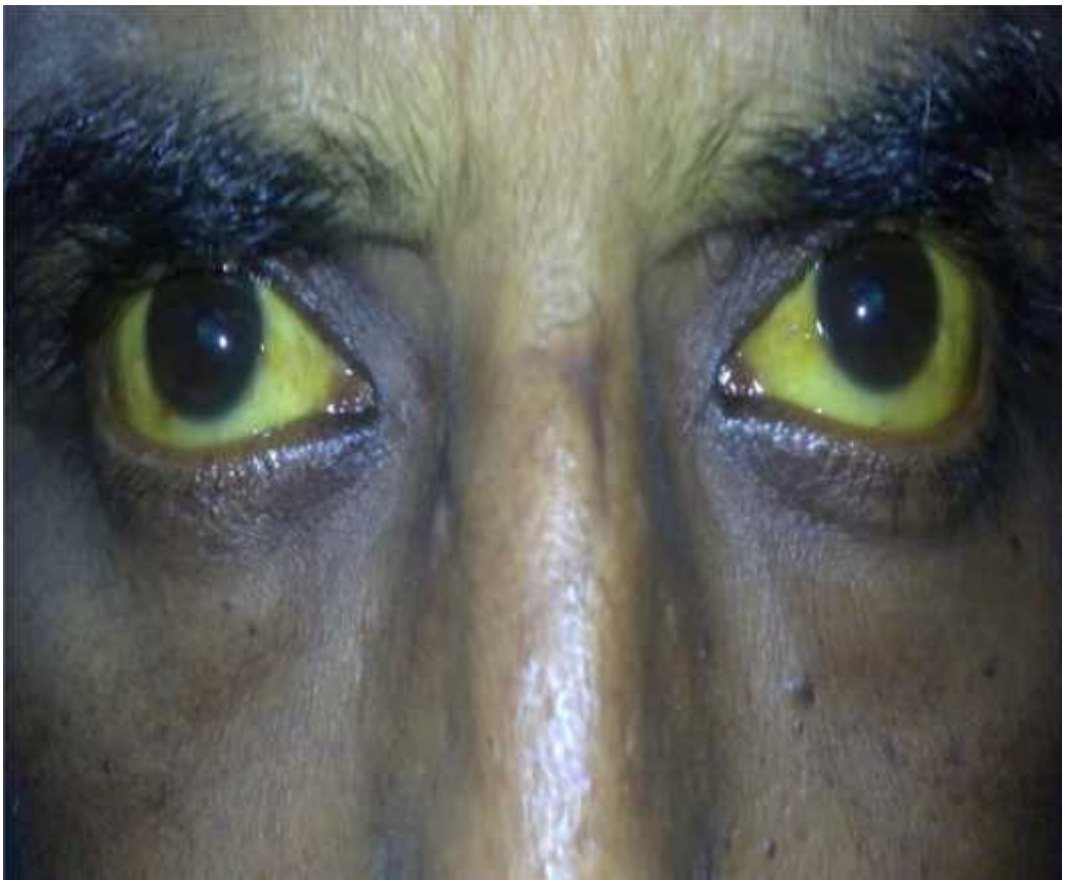

Figure 8 : (Man With Hyperbillirubinemia In P.Vivax Malaria)

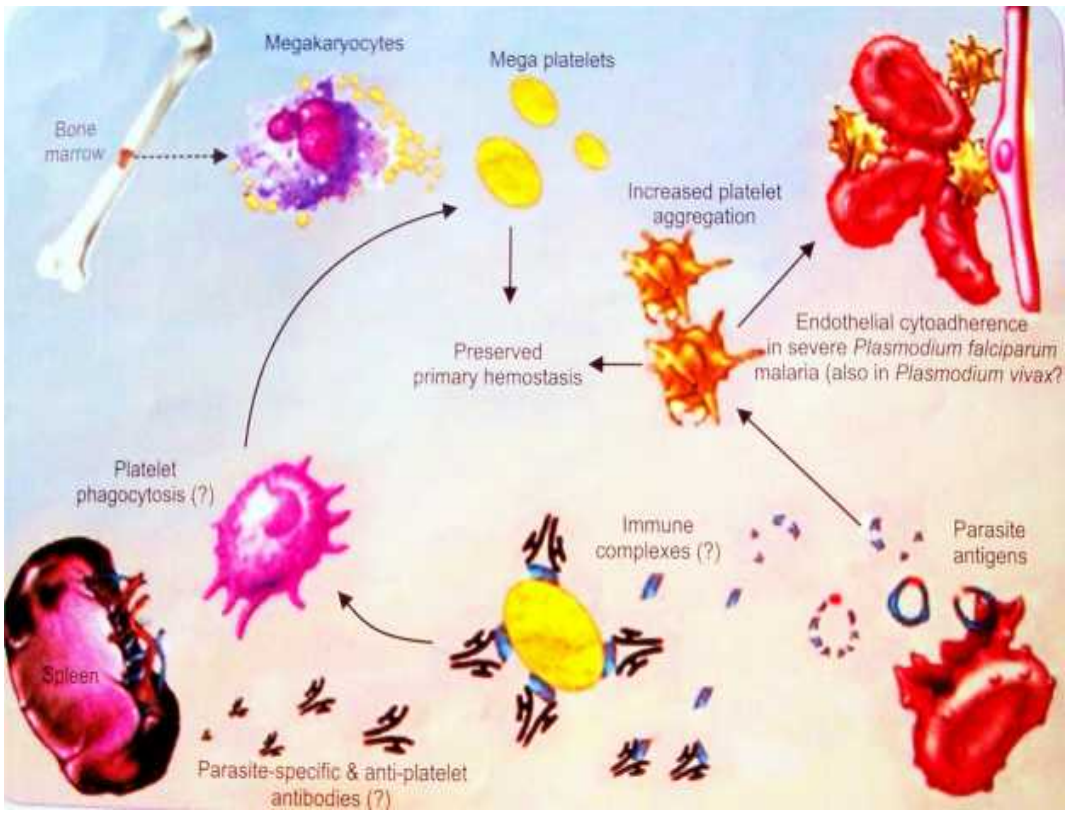

Figure 9 : Mechanisms Of Thrombocytopenia

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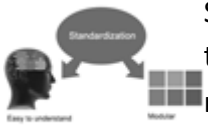

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To avoid postal delays, all transaction is preferred by e-mail. A finished manuscript submission is confirmed by e-mail immediately and your paper enters the editorial process with no postal delays. When a conclusion is made about the publication of your paper by our Editorial Board, revisions can be submitted online with the same procedure, with an occasion to view and respond to all comments.

Complete support for both authors and co-author is provided.

4. MANUSCRIPT'S CATEGORY

Based on potential and nature, the manuscript can be categorized under the following heads:

Original research paper: Such papers are reports of high-level significant original research work.

Review papers: These are concise, significant but helpful and decisive topics for young researchers.

Research articles: These are handled with small investigation and applications

Research letters: The letters are small and concise comments on previously published matters.

5.STRUCTURE AND FORMAT OF MANUSCRIPT

The recommended size of original research paper is less than seven thousand words, review papers fewer than seven thousands words also.Preparation of research paper or how to write research paper, are major hurdle, while writing manuscript. The research articles and research letters should be fewer than three thousand words, the structure original research paper; sometime review paper should be as follows:

Papers: These are reports of significant research (typically less than 7000 words equivalent, including tables, figures, references), and comprise:

(a)Title should be relevant and commensurate with the theme of the paper.

(b) A brief Summary, "Abstract" (less than 150 words) containing the major results and conclusions.

(c) Up to ten keywords, that precisely identifies the paper's subject, purpose, and focus.

(d) An Introduction, giving necessary background excluding subheadings; objectives must be clearly declared.

(e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition; sources of information must be given and numerical methods must be specified by reference, unless non-standard.

(f) Results should be presented concisely, by well-designed tables and/or figures; the same data may not be used in both; suitable statistical data should be given. All data must be obtained with attention to numerical detail in the planning stage. As reproduced design has been recognized to be important to experiments for a considerable time, the Editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned un-refereed;

(g) Discussion should cover the implications and consequences, not just recapitulating the results; conclusions should be summarizing.

(h) Brief Acknowledgements.

(i) References in the proper form.

Authors should very cautiously consider the preparation of papers to ensure that they communicate efficiently. Papers are much more likely to be accepted, if they are cautiously designed and laid out, contain few or no errors, are summarizing, and be conventional to the approach and instructions. They will in addition, be published with much less delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and to make suggestions to improve briefness.

It is vital, that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

Format

Language: The language of publication is UK English. Authors, for whom English is a second language, must have their manuscript efficiently edited by an English-speaking person before submission to make sure that, the English is of high excellence. It is preferable, that manuscripts should be professionally edited.

Standard Usage, Abbreviations, and Units: Spelling and hyphenation should be conventional to The Concise Oxford English Dictionary. Statistics and measurements should at all times be given in figures, e.g. 16 min, except for when the number begins a sentence. When the number does not refer to a unit of measurement it should be spelt in full unless, it is 160 or greater.

Abbreviations supposed to be used carefully. The abbreviated name or expression is supposed to be cited in full at first usage, followed by the conventional abbreviation in parentheses.

Metric SI units are supposed to generally be used excluding where they conflict with current practice or are confusing. For illustration, 1.4 l rather than 1.4 × 10-3 m3, or 4 mm somewhat than 4 × 10-3 m. Chemical formula and solutions must identify the form used, e.g. anhydrous or hydrated, and the concentration must be in clearly defined units. Common species names should be followed by underlines at the first mention. For following use the generic name should be constricted to a single letter, if it is clear.

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Abstract, used in Original Papers and Reviews:

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Key Words

A major linchpin in research work for the writing research paper is the keyword search, which one will employ to find both library and Internet resources.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy and planning a list of possible keywords and phrases to try.

Search engines for most searches, use Boolean searching, which is somewhat different from Internet searches. The Boolean search uses "operators," words (and, or, not, and near) that enable you to expand or narrow your affords. Tips for research paper while preparing research paper are very helpful guideline of research paper.

Choice of key words is first tool of tips to write research paper. Research paper writing is an art.A few tips for deciding as strategically as possible about keyword search:

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- It may take the discovery of only one relevant paper to let steer in the right keyword direction because in most databases, the keywords under which a research paper is abstracted are listed with the paper.
- One should avoid outdated words.

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Acknowledgements: Please make these as concise as possible.

References

References follow the Harvard scheme of referencing. References in the text should cite the authors' names followed by the time of their publication, unless there are three or more authors when simply the first author's name is quoted followed by et al. unpublished work has to only be cited where necessary, and only in the text. Copies of references in press in other journals have to be supplied with submitted typescripts. It is necessary that all citations and references be carefully checked before submission, as mistakes or omissions will cause delays.

References to information on the World Wide Web can be given, but only if the information is available without charge to readers on an official site. Wikipedia and Similar websites are not allowed where anyone can change the information. Authors will be asked to make available electronic copies of the cited information for inclusion on the Global Journals Inc. (US) homepage at the judgment of the Editorial Board.

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TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

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3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

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11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

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18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

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20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

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33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

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Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

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· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

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Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

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The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

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- Fundamental goal
- To the point depiction of the research
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- Significant conclusions or questions that track from the research(es)

Approach:

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The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

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- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
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Approach:

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- Explain materials individually only if the study is so complex that it saves liberty this way.
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- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

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- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

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- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

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- Resources and methods are not a set of information.
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- Leave out information that is immaterial to a third party.

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The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
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- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

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- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
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- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

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References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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