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Inside

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Glucose -6-phosphate dehydrogenase (G6PD) deficiency

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Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme that catalyses the first reaction in the hexose mono phosphate pathway (HMP) in which glucose is converted into the pentose sugars required for glycolysis and various biosynthetic reactions. G6PD oxidizes glucose-6-phosphate to 6-phosphogluconolactone with the simultaneous reduction of NADP to NADPH. This NADPH is essential for the reduction of oxidized glutathione to the reduced state of glutathione (GSH), as well as for the reduction of mixed disulphides of glutathione and cellular proteins[1]. GSH is necessary for the removal of red cell oxidants, such as superoxide anion (O_2^-) and hydrogen peroxide (H_2O_2). Accumulation of these oxidants may reduce the life span of the erythrocyte by accelerating the rate of oxidation of erythrocyte proteins including haemoglobin, plasma membrane proteins and enzymes. G6PD is present in all cells. However, its concentration varies in different tissues[2]. In the erythrocytes, the HMP is the only source of NADPH. If NADPH cannot be maintained, GSH levels fall and oxidative damage occurs resulting ultimately in hemolysis. Therefore, defence against oxidative damage is dependent on G6PD[3] and the main function of the HMP in erythrocytesis seems to be to protect the RBC against oxidative damage[4].

The G6PD gene is located at the telomeric region at the long arm of the X chromosome (band Xq28) which is close to the genes for haemophilia A, congenital dyskeratosis and colour blindness. The G6PD gene spans 18 kb on the X chromosome (xq28) and contains 13 exons. Males have only one G6PD gene (hemizygous for this gene) and they may be either normal or G6PD-deficient. Females have two G6PD genes and they can be either normal or deficient (homozygous) or intermediate (heterozygous). Heterozygous females are genetic mosaics as a result of X-chromosome inactivation (in any cell, one X chromosome is inactive but different cells randomly inactivate one chromosome or the other) and the abnormal cells of a heterozygous female can be deficient for G6PD as G6PD-deficient male. Such females can be susceptible to the same pathophysiological phenotype[5]. Although heterozygous women on average have less severe clinical manifestations than G6PD-deficient males, some develop severe acute haemolytic anaemia[6].

All mutations of the G6PD gene that result in enzyme deficiency affect the coding sequence[7]. About 140 mutations have been reported and most of which are single-base substitutions leading to amino acid replacements.

Deficient G6PD alleles are distributed worldwide. At least 400 million people carry a mutation in the G6PD gene causing deficiency [8-9]. The highest frequencies are detected in Africa, Asia, the Mediterranean region and in the middle east. Because of recent migration, the disorder is also found in North and South America and in northern European countries [10].

Most G6PD-deficient individuals are asymptomatic throughout their life and unaware of their status. The illness generally manifests as acute haemolysis which generally arises when red blood cells undergo oxidative stress triggered by agents such as drugs, infection or the ingestion of fava beans. G6PD deficiency does not seem to affect life expectancy, quality of life or the activity of affected individuals [11-12].G6PD deficiency usually presents as drug-induced or infection-induced acute haemolytic anaemia, favism, neonatal jaundice, or chronic non-spherocytic haemolytic anaemia.
Variants of G6PD deficiency were grouped into five classes based on enzyme activity and clinical manifestations [13].
Class I: Severely deficient, associated with chronic non-spherocytic haemolytic anaemia (CNSHA)
Class II: Severely deficient (1-10% residual activity), associated with acute haemolytic anaemia
Class III: Moderately deficient (10-60% residual activity)
Class IV: Normal activity (60-150%)
Class V: Increased activity (>150%)
Variants can also be classified as sporadic or polymorphic [3]. Polymorphic G6PD variants also known as WHO class II and III[14] and these are those that have reached noticeable gene frequencies (1-70%) in particular populations. Different geographical areas have different sets of polymorphic variants. It is now established that the high frequency of polymorphic variants has arisen because G6PD deficiency gives a relative protection against severe malaria[15-16]. Sporadic variants causing CNSHA (also known as WHO class I) occur at a very low frequency in any part of the world. Prevalence of G6PD deficiency in the Indian community was first reported from the Parsi population of Mumbai in the year 1963 by Baxi et al[17]. The prevalence rate of G6PD deficiency varies between 0-28% in different caste, tribe and ethnic Groups. The highest frequency (27.94%) has been reported from Vataliya Prajapati from Surat, Gujarat[18, 19]. In Madhya Pradesh, prevalence of G6PD deficiency varies between 0-5% in caste and tribal groups. In primitive tribes like Baiga and Bharia of Madhya Pradesh, prevalence of G6PD deficiency is up to 9% [20].

The mechanism of the protection against severe malaria is not known but some studies suggest that parasite infected G6PD deficient red blood cells are removed from the circulation by phagocytosis [21]. Red blood cells infected by malaria produce massive amounts of oxidizing agents as hemoglobin is degraded in the food vacuole of the parasite, deficient cells are rapidly damaged and phagocytosed along with their parasites.

The definitive diagnosis of G6PD deficiency is based on the estimation of enzyme activity by quantitative spectrophotometric analysis of the rate of NADPH production from NADP [22]. For rapid population screening, several semiquantitative methods have been applied, such as the dye-decolouration test developed by Motulsky in 1961 and fluorescent spot tests which indicate G6PD deficiency when the blood spot fails to fluoresce under ultraviolet light [23]. Diagnostic issues can arise for G6PD variants when measuring enzyme activity during an episode of acute haemolysis, or in the presence of a high reticulocyte count, because the level of activity in young erythrocytes is higher than in more mature cells, leading to false negative results for G6PD deficiency[24]. Diffi culties can also be encountered in the assessment of neonates who have a young red-blood-cell population. Diagnosis of heterozygous females may be difficult because X-chromosome inactivation[25-27]. Heterozygotes have two RBC populations one of these populations consists of normal RBCs and the other of RBCs that are as deficient as those of a homozygous male with the same deficient variant. Molecular analysis is the only method by which a definitive diagnosis can be made of a female's status.

The development of a number of PCR-based methods for the detection of known mutations in G6PD has made it possible to detect G6PD deficiency and to identify the specific mutation responsible with relative ease. The advantage of the use of this type of technology is that DNA samples are much more stable than the enzyme in blood samples, and that very small volumes suffice for diagnosis.

Diagnosis should be considered in children with a family history of jaundice, anemia, plenomegaly or cholelithiasis especially in those of Mediterranean or African ancestry [28]. Testing should be considered in children and adults with an acute hemolytic reaction caused by infection, exposure to a known oxidative drug, or ingestion of fava beans.

The management strategy for G6PD deficiency is to prevent haemolysis by avoiding oxidative stressors such as drugs and fava beans. This requires the patient to be aware of their deficiency by previous haemolytic episode or a screening. Usually acute haemolysis in deficient individuals is short-lived and does not need specific treatment. Rarely in children, does acute haemolysis lead to severe anaemia that requires blood transfusion.

In areas of high prevalence, clinicians and patients must be prepared to avoid any factors that might trigger severe clinical manifestations of the deficiency. If clinical and haematological findings are indicative of G6PD deficiency, this should be confirmed by quantitative spectrophotometric measurement of red blood cell enzyme activity. Neonates should be tested for G6PD deficiency if they have a family history of haemolysis or they are of a particular ethnic/geographic origin. If they have neonatal jaundice, that suggests the possibility of G6PD deficiency. It has been suggested that universal screening should be undertaken in countries with a high prevalence of G6PD deficiency and is already established in parts of South East Asia, the Middle East and Eastern Europe. Detection of G6PD deficiency identifies those at risk of neonatal jaundice which allow counselling of parents regarding avoidance of triggers. Selective testing for G6PD deficiency should be undertaken in newborns with unexplained or prolonged jaundice

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Publications

1. Kumar D & Sehgal V.K. Effect of endogenous and exogenous variables in infant health: A rank correlation analysis. Journal of Social Anthropology, Page11-19, Vol.7, No.1-2, 2010. (Published in February 2012)

2. Kumar D. Knowledge and practices of maternal health care among Baigas of Dindori, Madhya Pradesh; RMRCT, UPDATE, Vol.7, No.2, October 2010. (Published in February 2012)

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8. Tapas Chakma, P Vinay Rao, Pradeep Meshram. Factors associated with high compliance during Iron Folic Acid (IFA) supplementation in a tribal area of Madhya Pradesh, India. Published in Public Health Nutrition. 2012. Doi: 10.1017/S1368980012002704.

Conference/Workshop/ Meeting attended

Dr. Neeru Singh

1. Attended Vector forum meeting at Delhi and made presentation on Anopheles culicifacies on 4th & 5th Oct.'11.
2. Attended meeting of National society of Parasitology on 19-20 Nov. '11 at Chennai.
3. Attended DST meeting on 20 - 21 Nov'11 on environment and presented paper on vector borne disease with special reference to environment change.
4. Attended ICMR tribal health forum meeting at NIH Bombay on 6th Dec.'11.
5. Attended NVBDCP meeting on Bivalent kit on 23rd Dec.,11 at Delhi.
6. Attended conference on reproductive health and delivered a lecture on MIP on 20th Feb'12.
7. Attended Diagnostic meeting on 21st Feb'12 at NIE, New Delhi.
8. Attended meeting on Iron and malaria at NIH USA from 7th to 16th Feb. 2012.
9. Attended tribal health forum meeting on 4th March'12 in Hyderabad.
10. Attended meeting on 26th & 27th Mar'12 with DG at Delhi on NC Drink factor.

Dr. R.S. Balgir

1. Presented paper in Inter-Congress of Indian National Confederation and Academy of Anthropologists held during 21st to 23rd February 2012 at Department of Anthropology, University of Lucknow, Lucknow.
2. Presented paper presented in the International Conference on Genes, Genetics & Genomics: Today & Tomorrow - Human Concerns and 37th Annual Conference of the Indian Society of Human Genetics held during 3-5th March 2012 at Panjab University, Chandigarh.
3. Delivered an lecture on 12th March 2012 and interacted with students and faculty members at Department of Anthropology and Tribal Development, Guru Ghasidas Vishwavidyalaya, Bilaspur, Chhattisgarh.
4. Presented paper in the National Seminar-cum-Workshop on "Health Status and Developmental Health Strategies of Tribal Children of Chhattisgarh State" organized during 15-17 March 2012 at Tribal Research and Training Institute, Raipur, Chhattisgarh.
5. Delivered an lecture in the National Seminar on Tribal Health and Genomics held during March 19-21, 2012 at the Centre for Genomics, Jiwaji University, Gwalior.

Dr.V.G.Rao

1. Third South Central and 13th MP state chapter of Indian Association of Preventive & Social Medicine (IAPSM) joint Conference organized by Department of Community Medicine, NSCB Medical College, Jabalpur (MP), at Jabalpur during 11 - 13 Nov., 2011.
2. Seminar on Bovine Tuberculosis organized by Vet. College, Jabalpur at Jabalpur on 14th Dec. 2011.
3. Presented paper in International Science Symposium on HIV & Infectious Diseases organized by YRG Centre for AIDS Research and Education, Chennai, at Chennai during 20th -22nd January 2012.
4. Presented paper in National Seminar on Tribal Health and Genomics organized by Centre for Genomics, Jiwaji University, Gwalior at Gwalior during 19th -21st March, 2012.

Dr. Tapas Chakma

1. Attended meeting on expert group on Hypertension at ICMR Head quarter on 11th November 2011.
2. Delivered a lecture on the "Health effects of fluorosis" to medical officers of Seoni District under National Programme for fluorosis Prevention and Control on 23rd November 2011 organised by CMHO Seoni.
3. Attended Meeting on ICMR forum on tribal health held at NIIH Mumbai on 6th December 2011.
4. Delivered lectures to medical officers of Mandla District under National Programme for fluorosis Prevention and Control on 9th January 2012 organised by CMHO Mandla.
5. Attended fluorosis sub group meeting on the Researchable issues in fluorosis at ICMR head quarter on 19th January 2012.
6. Attended a workshop on "Challenges of Rural Water supplies in India" and delivered a lecture on the health effects of fluorosis and Role of nutrition on fluorosis mitigation organized by PHED Bhopal on 10th February 2012.
7. Attended an International workshop on "Mitigating effects of Geogenic Contaminants" and delivered a lecture on the "Role of nutrition on fluorosis mitigation" on 22nd and 23rd February 2012, organized by NEERI, Nagpur.

8. Attended fluorosis sub group meeting on the Researchable issues in fluorosis at ICMR head quarter on 15th March 2012.

Dr. K.B.Saha

1. Appeared for Talk show on 23 August 2011 on the topic Rural Health at ALL India Radio, Jabalpur and the same broadcasted on 21st October 2011.
2. Attended and presented a paper at the National Conference on Tribal Health: Issues and challenges, organized by the Department of Anthropology & Tribal Studies, Bastar Vishwavidyalaya, Jagdalpur, Chhattisgarh on 15-16 October 2011.
3. Attended a Face to Face contact programme on the online PG Diploma course on Bioethics by ICMR-IGNOU supported by NIH, USA at St. Johns Academy of Medical Sciences, Bangalore on 20-24 February 2012.

Dr. Jyothi Bhat

1. Attended Training on 'Lucipherase reporter phage assay' at NIRT, Chennai from 8th to 10th September 2011.
2. Presented a paper entitled 'Etiology of diarrhoeal diseases in tribal population of M.P' in XI Symposium on Vectors and Vector Borne Diseases, held at RMRCT, Jabalpur during 15th -17th October 2011.
3. Attended Collaborative Indo Swedish Public Health Initiative for Research Excellence (INSPIRE) Project meeting held at Karolinska Institute, Stockholm, Sweden from 25th to 27th January 2012.
4. Attended Workshop on National Rotavirus Surveillance Network at CMC, Vellore from 5th to 7th March 2012.
5. Presented a paper entitled 'Drug resistant tuberculosis among tribal population of Madhya Pradesh' in National Seminar on Tribal Health and Genomics held at Jiwaji University Gwalior during 19th to 21st March 2012.

Dr. Surendra Kumar

1. Attended health camp and awareness program on request for Regional Publicity officer Jabalpur and delivered a lecture on Tobacco related disease and its prevention, 8th December 2011 at Halka, 14th December 2011 at chorikala, 27th January 2012 at Lahser village, Jabalpur district.
2. Attended a workshop on Application of Statistical Software in Medical Research Institute of Cytology and Preventive Oncology (ICPO) ICMR 1-7, Sector - 39 NOIDA (UP) 18th to 20th January 2012.
3. Attended National Rotavirus Surveillance Network Workshop CMC Vellore, 5th to 7th March 2012.

Dr. Dinesh Kumar

1. Attended National Workshop on 'Statistical Epidemiology' in the Department of Statistics, Manipal University during 1st-5th August, 2011.

Dr. R.K.Sharma

1. Presented a paper in XI Symposium on Vectors and Vector Borne Diseases, held at RMRCT, Jabalpur during 15th -17th October 2011.

Dr. Pradip Barde

1. Attended 10 days Bioinformatics workshop on the molecular evolution of Influenza viruses at the National Institute of Virology, Pune, jointly organized by NIV Pune and CDC, Atlanta in May 2011.

Mr. Subash Godbole

1. Presented poster titled Detection of Dengue 4 from Jabalpur, Madhya Pradesh. at XI Symposium on Vectors & Vector Borne Diseases, Jabalpur during 15th -17th October 2011.

Mr. L S Kaushal

1. Presented poster titled Dengue Activity in Jabalpur: Serological evidence, at XI Symposium on Vectors & Vector Borne Diseases, Jabalpur, 15th -17th October 2011.

Workshops/Training/Meetings conducted

- Training for laboratory technicians of ICTC and Facility Integrated Counseling and testing centre (FICTC) was conducted in five batches during 19th to 23rd Dec, 26th to 30th Dec 2012, 16th to 20th Jan, 30th Jan to 3rd Feb, 6th to 10th Feb and 13th to 17th Feb 2012 in association with M.P. State AIDS Control Society at RMRCT. Hundred and two laboratory technicians were trained for HIV testing as per NACO modules.
- Workshop on External Quality Assurance Scheme (EQAS) was conducted for technicians of ICTC and blood banks on 2 occasions; 24th & 25th August and 16th and 17th December 2011.

- XI Symposium on Vectors and Vector Borne Diseases, held at RMRCT, Jabalpur during 15th -17th October 2011. All scientists, staff and students of the centre participated in different capacity in organizing the symposium.

- A two day work shop for training the medical officers on dengue and chikungunya of state government was organized wherein 10 officers participated.
- Biosafety training to ICTC Laboratory Technicians was provided in six training programme organized by microbiology department of the centre for NACO.
- Six training workshops for malaria workers & Four training workshops for Medical Officers from various districts of Madhya Pradesh on vector borne diseases were organized during the period at RMRCT Jabalpur. The workshops were organized jointly by RMRCT/ NIMR FS Jabalpur and Directorate of Health Services Bhopal under Enhanced Vector Borne Disease Control Programme (EVBDCP).

Laboratories news

ICTC for HIV

Integrated Counseling and Testing Centre at RMRCT is providing counseling and testing for HIV under NACO. Total of 2981 individuals were tested for HIV this year. The positivity in males was 11% (158/1436) while in females it was 5.7% (88/1545).

Intermediate Reference Laboratory (IRL) for Tuberculosis

The Mycobacteriology laboratory of the centre was accredited as IRL by Central TB Division in 2010. In September 2011 DOTS Plus program was initiated in Jabalpur district. Presently the laboratory is linked to 6 districts and receives samples from these districts for culture and DST of TB. Till March 2012 the laboratory has received 34 samples from MDR suspected cases and 16 MDR have been detected.

Virology Laboratory

This laboratory is recognized as Apex Referral Laboratory (ARL) for dengue and chikungunya for the state of Madhya Pradesh and Chhattisgarh by National Vector Borne Disease Control Programme. Demonstrated, the presence of Dengue Virus 1, and 4 for first time from central India.

Joining/Retirement/Termination

- Smt. Pushpa Umate, Assistant: Terminated 16/12/2011
- Mrs. S. J. Khan, ARS: Retired on 31/12/2011
- Shri Avinash Dubey, Technician A: Joined on 24/01/2012
- Ms Sandhya Sharma, Stenographer: Joined on 24/01/2012
- Shri Rameshwar Prasad Attendant (Services): Retired on 31/01/2012
- Shri G. P. Shukla, Technical Assistant: Retired on 29/2/2012

Award/ Honour

- Dr. Neeru Singh, Scientist G & Director of the centre nominated as a member of steering committee on Empowerment of Scheduled Tribes (STs), Planning Commission, Delhi.
- Dr. Neeru Singh invited as member of the India Country Coordination Mechanism for the Global Fund representing the Academic and Research Constituency for Malaria seat.
- Dr. Neeru Singh elected as a Fellow of The National Academy of Sciences, India (NASI), Allahabad.

Events

- **Inauguration of new guest house**

  The Secretary, DHR, Govt of India & DG, ICMR inagurated New guest house on 15th October 2011.

- **Symposium on vector and vector borne diseases**

  XI Symposium on vector and vector borne diseases was organized by centre during 15th- 17th October 2011. The Secretary, DHR, Govt of India & DG, ICMR inagurated the Symposium on 15th October 2011.

- **National vigilance week** (5th-9th November 2011)

  All the employees of the centre took oath during the national vigilance week.

- **SAC Meeting** (5th January 2012)

  24th Scientific Advisory Committee meeting was held at the centre on 5th January 2012. Work done by the centre during the year was reviewed by eminent members.

- **Republic day** (26th January 2012)

  63rd republic day of the country was celebrated with great enthusiasm.

- **Foundation day** (1st March 2012)

  29th foundation day of the centre was celebrated on 1st March 2012. The foundation day lecture was delivered by Dr. Lokwani, Vice chancellor of Medical University, Jabalpur.