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Autosomal Recessive Disorders and X Linked Disorders in Malaysia

See full search strategy

1. International perspectives on the implementation of reproductive carrier screening.

Author(s): Delatycki, Martin B; Alkuraya, Fowzan; Archibald, Alison; Castellani, Carlo; Cornel, Martina; Grody, Wayne W; Henneman, Lidewij; Ioannides, Adonis S; Kirk, Edwin; Laing, Nigel; Lucassen, Anneke; Massie, John; Schuurmans, Juliette; Thong, Meow-Keong; van Langen, Irene; Zlotogora, Joël

Source: Prenatal diagnosis; Nov 2019

Publication Date: Nov 2019

Publication Type(s): Journal Article Review

PubMedID: 31774570

Available at Prenatal diagnosis - from Wiley Online Library

Abstract: Reproductive carrier screening started in some countries in the 1970s for hemoglobinopathies and Tay-Sachs disease. Cystic fibrosis carrier screening became possible in the late 1980s and with technical advances, screening of an ever increasing number of genes has become possible. The goal of carrier screening is to inform people about their risk of having children with autosomal recessive and X-linked recessive disorders, to allow for informed decision making about reproductive options. The consequence may be a decrease in the birth prevalence of these conditions, which has occurred in several countries for some conditions. Different programs target different groups (high school, premarital, couples before conception, couples attending fertility clinics, and pregnant women) as does the governance structure (public health initiative and user pays). Ancestry-based offers of screening are being replaced by expanded carrier screening panels with multiple genes that is independent of ancestry. This review describes screening in Australia, Cyprus, Israel, Italy, Malaysia, the Netherlands, Saudi Arabia, the United Kingdom, and the United States. It provides an insight into the enormous variability in how reproductive carrier screening is offered across the globe. This largely relates to geographical variation in carrier frequencies of genetic conditions and local health care, financial, cultural, and religious factors.

Database: Medline

2. Clinical, biochemical and genetic profiles of patients with mucopolysaccharidosis type IVA (Morquio A syndrome) in Malaysia: The first national natural history cohort study

Author(s): Leong H.Y.; Chew H.B.; Keng W.T.; Md Haniffa M.A.; Ngu L.H.; Abdul Azize N.A.; Mohd Khalid M.K.N.; Yakob Y.; Thong M.K.; Hung L.C.; Mohamed Zainudin N.; Ramlee A.

Source: Orphanet Journal of Rare Diseases; Jun 2019; vol. 14 (no. 1)

Publication Date: Jun 2019

Publication Type(s): Article

PubMedID: 31200731

Available at Orphanet journal of rare diseases - from BioMed Central

Available at Orphanet journal of rare diseases - from SpringerLink - Medicine

Abstract: Background: Mucopolysaccharidosis IVA (MPS IVA) is an autosomal recessive lysosomal storage disease due to N-acetylgalactosamine-6-sulfatase (GALNS) deficiency. It results in accumulation of the glycosaminoglycans, keratan sulfate and chondroitin-6-sulfate, leading to skeletal and other systemic impairments. Data on MPS IVA in Asian populations are scarce. Method(s): This is a multicentre descriptive case series of 21 patients comprising all MPS IVA patients in Malaysia. Mutational analysis was performed by PCR and Sanger sequencing of the GALNS gene in 17 patients. Result(s): The patients (15 females and 6 males) had a mean age (+/- SD) of 15.5 (+/- 8.1) years. Mean age at symptom onset was 2.6 (+/- 2.1) years and at confirmed diagnosis was 6.9 (+/- 4.5) years. The study cohort included patients from all the main ethnic groups in Malaysia - 57% Malay, 29% Chinese and 14% Indian. Common presenting symptoms included pectus carinatum (57%) and genu valgum (43%). Eight patients (38%) had undergone surgery, most commonly knee surgeries (29%) and cervical spine decompression (24%). Patients had limited endurance with lower mean walking distances with increasing age. GALNS gene analysis identified 18 distinct mutations comprising 13 missense, three nonsense, one small deletion and one splice site mutation. Of these, eight were novel mutations (Tyr133Ser, Glu158Valfs*12, Gly168*, Gly168Val, Trp184*, Leu271Pro, Glu320Lys, Leu508Pro). Mutations in exons 1, 5 and 9 accounted for 51% of the mutant alleles identified. Conclusion(s): All the MPS IVA patients in this study had clinical impairments. A better understanding of the natural history and the clinical and genetic spectrum of MPS IVA in this population may assist early diagnosis, improve management and permit timely genetic counselling and prenatal diagnosis.

Database: EMBASE

3. Mutational Profiles of F8 and F9 in a Cohort of Haemophilia A and Haemophilia B Patients in the Multi-ethnic Malaysian Population.

Author(s): Zahari, Maimiza; Sulaiman, Siti Aishah; Othman, Zulhabri; Ayob, Yasmin; Karim, Faraizah Abd; Jamal, Rahman

Source: Mediterranean journal of hematology and infectious diseases; 2018; vol. 10 (no. 1); p. e2018056

Publication Date: 2018

Publication Type(s): Journal Article

PubMedID: 30210749

Available at Mediterranean journal of hematology and infectious diseases - from Europe PubMed Central - Open Access

Abstract: BackgroundHaemophilia A (HA) and Haemophilia B (HB) are X-linked blood disorders that are caused by various mutations in the factor VIII (F8) and factor IX (F9) genes respectively. Identification of mutations is essential as some of the mutations are associated with the development of inhibitors. This study is the first comprehensive study of the F8 mutational profile in Malaysia.Materials and methodsWe analysed 100 unrelated HA and 15 unrelated HB patients for genetic alterations in the F8 and F9 genes by using the long-range PCR, DNA sequencing, and the multiplex-ligation-dependent probe amplification assays. The prediction software was used to confirm the effects of these mutations on factor VIII and IX proteins.Results44 (53%) of the severe HA patients were positive for F8 intron 22 inversion, and three (3.6%) were positive for intron one inversion. There were 22 novel mutations in F8, including missense (8), frameshift (9), splice site (3), large deletion (1) and nonsense (1) mutations. In HB patients, four novel mutations were identified including the splice site (1), small deletion (1), large deletion (1) and missense (1) mutation.DiscussionThe mutational spectrum of F8 in Malaysian patients is heterogeneous, with a slightly higher frequency of intron 22 inversion in these severe HA patients when compared to other Asian populations. Identification of these mutational profiles in F8 and F9 genes among Malaysian patients will provide a useful reference for the early detection and diagnosis of HA and HB in the Malaysian population.

Database: Medline

4. Mutation Study of Malaysian Patients with Ornithine Transcarbamylase Deficiency: Clinical, Molecular, and Bioinformatics Analyses of Two Novel Missense Mutations of the OTC Gene

Author(s): Ali E.Z.; Zakaria Y.; Jusoh S.A.; Mohd Radzi M.A.; Ngu L.H.

Source: BioMed Research International; 2018; vol. 2018

Publication Date: 2018

Publication Type(s): Article

PubMedID: 30175132

Available at BioMed research international - from Europe PubMed Central - Open Access

Abstract: Ornithine transcarbamylase deficiency (OTCD), an X-linked disorder that results from mutations in the OTC gene, causes hyperammonemia and leads to various clinical manifestations. Mutations occurring close to the catalytic site of OTCase can cause severe OTCD phenotypes compared with those caused by mutations occurring on the surface of this protein. In this study, we report two novel OTC missense mutations, Q171H and N199H, found in Malaysian patients. Q171H and N199H caused neonatal onset OTCD in a male and late OTCD in a female, respectively. In silico predictions and molecular docking were performed to examine the effect of these novel mutations, and the results were compared with other 30 known OTC mutations. In silico servers predicted that Q171H and N199H, as well as 30 known missense mutations, led to the development of OTCD. Docking analysis indicated that N-(phosphonoacetyl)-L-ornithine (PALO) was bound to the catalytic site of OTCase mutant structure with minimal conformational changes. However, the mutations disrupted interatomic interactions in the catalytic site. Therefore, depending on the severity of disruption occurring at the catalytic site, the mutation may affect the efficiency of mechanism and functions of OTCase.

Database: EMBASE

5. Fourteen new mutations of BCKDHA, BCKDHB and DBT genes associated with maple syrup urine disease (MSUD) in Malaysian population.

Author(s): Ali, Ernie Zuraida; Ngu, Lock-Hock

Source: Molecular genetics and metabolism reports; Dec 2018; vol. 17 ; p. 22-30

Publication Date: Dec 2018

Publication Type(s): Journal Article

PubMedID: 30228974

Available at Molecular Genetics and Metabolism Reports - from Europe PubMed Central - Open Access

Abstract: Maple syrup urine disease (MSUD) is a rare autosomal recessive metabolic disorder. This disorder is usually caused by mutations in any one of the genes; BCKDHA, BCKDHB and DBT, which represent E1α, E1β and E2 subunits of the branched-chain α-keto acid dehydrogenase (BCKDH) complex, respectively. This study presents the molecular characterization of 31 MSUD patients. Twenty one mutations including 14 new mutations were identified. The BCKDHB gene was the most commonly affected (45.2%) compared to BCKDHA gene (16.1%) and DBT gene (38.7%). In silico webservers predicted all mutations were disease-causing. In addition, structural evaluation disclosed that all new missenses in BCKDHA, BCKDHB and DBT genes affected stability and formation of E1 and E2 subunits. Majority of the patients had neonatal onset MSUD (26 of 31). Meanwhile, the new mutation; c.1196C > G (p.S399C) in DBT gene was noted to be recurrent and found in 9 patients. Conclusion: Our findings have expanded the mutational spectrum of the MSUD and revealed the

genetic heterogeneity among Malaysian MSUD patients. We also discovered the p.S399C from DBT gene was noted as a recurrent mutation in Malay community and it suggested the existence of common and unique mutation in Malay population.

Database: Medline

6. Comparison of gene mutation spectrum of thalassemia in different part of China and Southeast Asia

Author(s): Zhuo Y.; Ling Q.; Quexuan C.; Wenzhe Z.; Bing H.

Source: HemaSphere; Jun 2018; vol. 2 ; p. 1099

Publication Date: Jun 2018

Publication Type(s): Conference Abstract

Abstract: Background: Thalassemia is a common genetic disorder. High prevalence of thalassemia is found in South China, Southeast Asia, India, Middle East and Mediterranean. Thalassemia is usually thought to exist only in southern China, but more and more cases from northern China have been reported recently. Aim(s): We compared gene spectrum of alpha and beta-thalassemia in northern and southern China in our group, and compared our data with the largest metaanalysis in southern China, and data from Southeast Asian countries. The results may help to understand the similarities and differences of people from different area and different ethnic groups. Method(s): During 2012 to 2017, suspected thalassemia people were detected for common alpha and beta-thalassemia mutations by gap-PCR and reverse dot blot (RDB) analysis in Peking Union Medical College hospital (PUMCH). 1059 people who carried thalassemia genes were analyzed retrospectively. We picked mutated individuals with northern identity card numbers and conducted telephone follow-up survey in order to collect their ancestral information. Besides, we used 'thalassemia', 'mutation', and Southeast Asian countries as keywords to search potential related studies in PubMed and EMbase. Result(s): All carriers included in our study resided in northern China. Among them, 17.3% were native northerners and 82.7% were immigrants from southern China. Although significant difference was found between our data and data from the meta-analysis literature of southern China in both alpha and beta-thalassemia, we also found some similarities between them. Similar gene mutation spectrum were found between Malaysia Chinese and Guangdong people, while other ethnic people in Southeast Asia had totally different gene spectrum from that of Chinese people. Summary/Conclusion: Chinese People originated from north may have lower percentage of alpha-thalassemia mutations. Chinese people in different area had similar gene mutation profile and Chinese people had significantly different gene spectrum from other ethnic people in Southeast Asia.

Database: EMBASE

7. Molecular Characterisation of alpha- and beta-Thalassaemia among Indigenous Senoi Orang Asli Communities in Peninsular Malaysia

Author(s): Koh D.X.R.; Ismail E.; Raja Sabudin R.Z.A.; Hussin N.H.; Mohd Yusoff M.; Ahmad R.; Othman A.

Source: Annals of Human Genetics; Sep 2017; vol. 81 (no. 5); p. 205-212

Publication Date: Sep 2017

Publication Type(s): Article

PubMedID: 28620953

Available at Annals of human genetics - from Wiley Online Library

Available at Annals of human genetics - from IngentaConnect - Open Access

Abstract: Thalassaemia is a public health problem in Malaysia, with each ethnic group having their own common mutations. However, there is a lack on data on the prevalence and common mutations among the indigenous people. This cross-sectional study was performed to determine the common mutations of alpha- and beta-thalassaemia among the subethnic groups of Senoi, the largest Orang Asli group in Peninsular Malaysia. Blood samples collected from six Senoi subethnic groups were analysed for full blood count and haemoglobin analysis (HbAn). Samples with abnormal findings were then screened for alpha- and beta-globin gene mutations. Out of the 752 samples collected, 255 showed abnormal HbAn results, and 122 cases showing abnormal red cell indices with normal HbAn findings were subjected to molecular screening. DNA analysis revealed a mixture of alpha- and beta-globin gene mutations with 25 concomitant cases. The types of gene abnormalities detected for alpha-thalassaemia were termination codon (T>C) Hb CS (alphaCSalpha), Cd59 (G>A) haemoglobin Adana (Hb Adana) (alphaCd59alpha), initiation codon (ATG>A-G) (alphaIniCdalpha), two-gene deletion (-SEA), and single-gene 3.7-kb deletion (-alpha3.7). For beta-thalassaemia, there were Cd26 (G>A) Hb E (betaE), Cd19 (A>G) Haemoglobin Malay (Hb Malay) (betaCd19), and IVS 1-5 (G>C) (betaIVS 1-5).

Database: EMBASE

8. Molecular analysis of fragile X syndrome (FXS) among Malaysian patients with developmental disability.

Author(s): Ali, E Z; Yakob, Y; Md Desa, N; Ishak, T; Zakaria, Z; Ngu, L K; Keng, W T

Source: The Malaysian journal of pathology; Aug 2017; vol. 39 (no. 2); p. 99-106

Publication Date: Aug 2017

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 28866690

Available at The Malaysian journal of pathology - from ProQuest (Health Research Premium) - NHS Version

Abstract: Fragile X syndrome (FXS) is a neurodevelopmental disorder commonly found worldwide, caused by the silencing of fragile X mental retardation 1 (FMR1) gene on the X-chromosome. Most of the patients lost FMR1 function due to an expansion of cytosine-guanine-guanine (CGG) repeat at the 5' untranslated region (5'UTR) of the gene. The purpose of this study is to identify the prevalence of FXS and characterize the FMR1 gene CGG repeats distribution among children with developmental disability in Malaysia. Genomic DNA of 2201 samples from different ethnicities (Malays, Chinese, Indian and others) of both genders were PCR-amplified from peripheral blood leukocytes based on specific primers at 5'UTR of FMR1 gene. Full mutations and mosaics were successfully identified by triple methylation specific PCR (ms-PCR) and subsequently verified with FragilEase kit. The findings revealed for the first time the prevalence of FXS full mutation in children with developmental disability in Malaysia was 3.5%, a slightly higher figure as compared to other countries. Molecular investigation also identified 0.2% and 0.4% probands have permutation and intermediate alleles, respectively. The CGG repeats length observation showed 95% of patients had normal alleles within 11 to 44 CGG repeats; with 29 repeats found most common among Malays and Indians while 28 repeats were most common among Chinese. In conclusion, this is the first report of prevalence and characterisation of CGG repeats that reflects genetic variability among Malaysian ethnic grouping.

Database: Medline

9. Haemoglobinopathies in the indigenous population of the east Malaysian state of Sabah

Author(s): Mohd Pauzy L.H.; Esa E.; Yusoff Y.M.; Yao P.R.; Jamaludin N.A.; Zakaria Z.; Mokhri N.

Source: Malaysian Journal of Pathology; Aug 2016; vol. 38 (no. 2); p. 192

Publication Date: Aug 2016

Publication Type(s): Conference Abstract

Available at Malaysian Journal of Pathology - from ProQuest (Health Research Premium) - NHS Version

Abstract: Introduction: The aim of the study is to examine the distribution of haemoglobinopathies in the indigenous population of Sabah where thalassaemia is most prevalent in Malaysia. Method(s): A total of 645 blood samples were obtained from health clinics and hospitals all over Sabah for thalassaemia screening in the month of May 2013. High Performance Liquid Chromatography and Capillary Electrophoresis were used for analysing the haemoglobin subtypes. Result(s): The study included patients aged between 1 to 73 years old. The majority (97%; 624/645) were indigenous people and 94% of the total sample came from voluntary screening offered at primary care level via various government-promoted programs. 82% were female, mostly screened during their antenatal visit. 30% (193/645) of the sample were tested positive for; B-Thalassaemia trait (78%; 151/193), Hb E trait (10%; 20/193), Homozygous Hb E (2%; 4/193) and other haemoglobinopathies (7%; 13/193). The other 3% (5/193) of the abnormal results were inconclusive hence would require further

molecular analysis. Among all the indigenous people screened, the Kadazandusuns had the highest occurrence of haemoglobinopathies (35%; 87/250), followed by the Muruts (33%; 15/45), Malays (29%; 19/65), other races (26%; 46/180) and the Bajau people (23%; 19/84). Discussion(s): Thalassaemia is prevalent in the indigenous population of Sabah and most people are asymptomatic. Government health clinics play a crucial role in promoting greater awareness of the disease via campaigns and screening programs as they are easily accessible and oftentimes are the first point of contact with the community.

Database: EMBASE

10. Analysis of alpha1 and alpha2 globin genes among patients with hemoglobin Adana in Malaysia

Author(s): Lee T.Y.; Lai M.I.; Teh L.K.; George E.; Ismail P.; Ramachandran V.; Tan J.A.M.A.; Othman R.; Hussein N.H.

Source: Genetics and Molecular Research; Apr 2016; vol. 15 (no. 2)

Publication Date: Apr 2016

Publication Type(s): Article

PubMedID: 27173219

Available at Genetics and Molecular Research - from Free Medical Journals . com

Available at Genetics and Molecular Research - from Unpaywall

Abstract: Hemoglobin (Hb) Adana [HBA2: c179G>A (or HBA1); p.Gly60Asp] is a non-deletional alpha-thalassemia variant found in Malaysia. An improvement in the molecular techniques in recent years has made identification of Hb Adana much easier. For this study, a total of 26 Hb Adana alpha-thalassemia intermedia and 10 Hb Adana trait blood samples were collected from patients. Common deletional and non-deletional alpha-thalassemia genotypes were determined using multiplex gap polymerase chain reaction (PCR) and multiplex ARMS PCR techniques. Identification of the Hb Adana location on the alpha-globin gene was carried out using genomic sequencing and the location of the mutation was confirmed via restriction fragment length polymorphism-PCR. Among the 36 samples, 24 (66.7%) had the -alpha3.7/alphaCd59alpha mutation, while the -alpha3.7/alphaCd59alpha mutation accounted for 2 samples (5.6%) and the remaining 10 (27.8%) samples were alpha/alphaCd59alpha. All 36 samples were found to have the Hb Adana mutation on the a2-globin gene. The position of the alpha-globin gene mutation found in our cases was similar to that reported in Indonesia (16%) but not to that in Turkey (0.6%). Our results showed that the Hb Adana mutation was preferentially present in the a2-globin genes in Malays compared to the other ethnicities in Malaysia. Thus, the Malays might have similar ancestry based on the similarities in the Hb Adana position.

Database: EMBASE

11. Report on von willebrand disease in Malaysia

Author(s): Periayah M.H.; Halim A.S.; Mat Saad A.Z.; Yaacob N.S.; Abdul Karim F.

Source: Open Access Macedonian Journal of Medical Sciences; Mar 2016; vol. 4 (no. 1); p. 112-117

Publication Date: Mar 2016

Publication Type(s): Article

Available at Open Access Macedonian Journal of Medical Sciences - from Europe PubMed Central - Open Access

Available at Open Access Macedonian Journal of Medical Sciences - from Unpaywall

Abstract:BACKGROUND: Von Willebrand disease (vWD) is an inherited hemostatic disorder that affects the hemostasis pathway. The worldwide prevalence of vWD is estimated to be 1% of the general population but only 0.002% in Malaysia. AIM: Our present paper has been written to disclose the statistical counts on the number of vWD cases reported from 2011 to 2013. MATERIAL AND METHODS: This article is based on sociodemographic data, diagnoses and laboratory findings of vWD in Malaysia. A total of 92 patients were reported to have vWD in Malaysia from 2011 to 2013. RESULT(S): Sociodemographic-analysis revealed that 60% were females, 63% were of the Malay ethnicity, 41.3% were in the 19-44 year old age group and 15.2% were from Sabah, with the East region having the highest registered number of vWD cases. In Malaysia, most patients are predominately affected by vWD type 1 (77.2%). Factor 8, von Willebrand factor: Antigen and vWF: Collagen-Binding was the strongest determinants in the laboratory profiles of vWD. CONCLUSION(S): This report has been done with great interest to provide an immense contribution from Malaysia, by revealing the statistical counts on vWD from 2011-2013.

Database: EMBASE

12. Carbamoylphosphate synthetase 1 (CPS1) deficiency: clinical, biochemical, and molecular characterization in Malaysian patients.

Author(s): Ali, Ernie Zuraida; Khalid, Mohd Khairul Nizam Mohd; Yunus, Zabedah Md; Yakob, Yusnita; Chin, Chen Bee; Abd Latif, Kartikasalwah; Hock, Ngu Lock

Source: European journal of pediatrics; Mar 2016; vol. 175 (no. 3); p. 339-346

Publication Date: Mar 2016

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 26440671

Available at European journal of pediatrics - from SpringerLink - Medicine

Available at European journal of pediatrics - from ProQuest (Health Research Premium) - NHS Version

Abstract:UNLABELLEDCarbamoyl phosphate synthetase 1 (CPS1) deficiency is a rare autosomal recessive disorder of ureagenesis presenting as life-threatening hyperammonemia. In this study, we present the main clinical features and biochemical and molecular data of six Malaysian patients with CPS1 deficiency. All the patients have neonatal-onset symptoms, initially diagnosed as infections before hyperammonemia was recognized. They have typical biochemical findings of hyperglutaminemia, hypocitrullinemia, and low to normal urinary excretion of orotate. One neonate succumbed to the first hyperammonemic decompensation. Five neonatal survivors received long-term treatment consisting of dietary protein restriction and ammonia-scavenging drugs. They have delayed neurocognitive development of varying severity. Genetic analysis revealed eight mutations in CPS1 gene, five of which were not previously reported. Five mutations were missense changes while another three were predicted to create premature stop codons. In silico analyses showed that

these new mutations affected different CPS1 enzyme domains and were predicted to interrupt interactions at enzyme active sites, disturb local enzyme conformation, and destabilize assembly of intact enzyme complex.CONCLUSIONAll mutations are private except one mutation; p.Ile1254Phe was found in three unrelated families. Identification of a recurrent p.Ile1254Phe mutation suggests the presence of a common and unique mutation in our population. Our study also expands the mutational spectrum of the CPS1 gene.

Database: Medline

13. Non-Invasive DNA Sampling for Molecular Analysis of Beta-Thalassemia: Amiable Alternative Sampling Methods with Accurate Results for Pediatric Patients.

Author(s): Abd Rahim, Mohd Rashdan; Kho, Siew-Leng; Kuppusamy, Umah Rani; Tan, Jin-Ai Mary Anne

Source: Clinical laboratory; 2015; vol. 61 (no. 9); p. 1325-1330

Publication Date: 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 26554253

Abstract:BACKGROUNDBeta-thalassemia is the most common genetic disorder in Malaysia. Confirmation of the β-globin gene mutations involved in thalassemia is usually carried out by molecular analysis of DNA extracted from leukocytes in whole blood. Molecular analysis is generally carried out when affected children are around 1 - 2 years as clinical symptoms are expressed during this period. Blood taking at this age can be distressing for the child. High yield and pure DNA extracted from non-invasive sampling methods can serve as alternative samples in molecular studies for genetic diseases especially in pediatric cases.METHODSIn this study, mouthwash, saliva, and buccal cytobrush samples were collected from β-thalassemia major patients who had previously been characterized using DNA extracted from peripheral blood. DNA was extracted from mouthwash, saliva, and buccal cytobrush samples using the conventional inexpensive phenol-chloroform method and was measured by spectrophotometry for yield and purity. Molecular characterization of β-globin gene mutations was carried out using the amplification refractory mutation system (ARMS).RESULTSDNA extracted from mouthwash, saliva, and buccal cytobrush samples produced high concentration and pure DNA. The purified DNA was successfully amplified using ARMS. Results of the β-globin gene mutations using DNA from the three non-invasive samples were in 100% concordance with results from DNA extracted from peripheral blood.CONCLUSIONSThe conventional in-house developed methods for non-invasive sample collection and DNA extraction from these samples are effective and negate the use of more expensive commercial kits. In conclusion, DNA extracted from mouthwash, saliva, and buccal cytobrush samples provided sufficiently high amounts of pure DNA suitable for molecular analysis of β-thalassemia.

Database: Medline

14. Transfusion-dependent thalassemia in Northern Sarawak: a molecular study to identify different genotypes in the multi-ethnic groups and the importance of genomic sequencing in unstudied populations.

Author(s): Tan, Jin-Ai M A; Chin, Saw-Sian; Ong, Gek-Bee; Mohamed Unni, Mohamed N; Soosay, Ashley E R; Gudum, Henry R; Kho, Siew-Leng; Chua, Kek-Heng; Chen, Jang J; George, Elizabeth

Source: Public health genomics; 2015; vol. 18 (no. 1); p. 60-64

Publication Date: 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 25412720

Abstract:BACKGROUNDAlthough thalassemia is a genetic hemoglobinopathy in Malaysia, there is limited data on thalassemia mutations in the indigenous groups. This study aims to identify the types of globin gene mutations in transfusion-dependent patients in Northern Sarawak.METHODSBlood was collected from 32 patients from the Malay, Chinese, Kedayan, Bisayah, Kadazandusun, Tagal, and Bugis populations. The α- and β-globin gene mutations were characterized using DNA amplification and genomic sequencing.RESULTSTen β- and 2 previously reported α-globin defects were identified. The Filipino β-deletion represented the majority of the β-thalassemia alleles in the indigenous patients. Homozygosity for the deletion was observed in all Bisayah, Kadazandusun and Tagal patients. The β-globin gene mutations in the Chinese patients were similar to the Chinese in West Malaysia. Hb Adana (HBA2:c.179G>A) and the -α(3.7)/αα deletion were detected in 5 patients. A novel 24-bp deletion in the α2-globin gene (HBA2:c.95 + 5_95 + 28delGGCTCCCTCCCCTGCTCCGACCCG) was identified by sequencing. Co-inheritance of α-thalassemia with β-thalassemia did not ameliorate the severity of thalassemia major in the patients.CONCLUSIONThe Filipino β-deletion was the most common gene defect observed. Homozygosity for the Filipino β-deletion appears to be unique to the Malays in Sarawak. Genomic sequencing is an essential tool to detect rare genetic variants in the study of new populations.

Database: Medline

15. The first Malay database toward the ethnic-specific target molecular variation.

Author(s): Halim-Fikri, Hashim; Etemad, Ali; Abdul Latif, Ahmad Zubaidi; Merican, Amir Feisal; Baig, Atif Amin; Annuar, Azlina Ahmad; Ismail, Endom; Salahshourifar, Iman; Liza-Sharmini, Ahmad Tajudin; Ramli, Marini; Shah, Mohamed Irwan; Johan, Muhammad Farid; Hassan, Nik Norliza Nik; Abdul-Aziz, Noraishah Mydin; Mohd Noor, Noor Haslina; Nur-Shafawati, Ab Rajab; Hassan, Rosline; Bahar, Rosnah; Zain, Rosnah Binti; Yusoff, Shafini Mohamed; Yusoff, Surini; Tan, Soon Guan; Thong, Meow-Keong; Wan-Isa, Hatin; Abdullah, Wan Zaidah; Mohamed, Zahurin; Abdul Latiff, Zarina; Zilfalil, Bin Alwi; members of the Malaysian Node of the Human Variome Project

Source: BMC research notes; Apr 2015; vol. 8 ; p. 176

Publication Date: Apr 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 25925844

Abstract:BACKGROUNDThe Malaysian Node of the Human Variome Project (MyHVP) is one of the eighteen official Human Variome Project (HVP) country-specific nodes. Since its inception in 9(th) October 2010, MyHVP has attracted the significant number of Malaysian clinicians and researchers to participate and contribute their data to this project. MyHVP also act as the center of coordination for genotypic and phenotypic variation studies of the Malaysian population. A specialized database was developed to store and manage the data based on genetic variations which also associated with health and disease of Malaysian ethnic groups. This ethnic-specific database is called the Malaysian Node of the Human Variome Project database (MyHVPDb).FINDINGSCurrently, MyHVPDb provides only information about the genetic variations and mutations found in the Malays. In the near future, it will expand for the other Malaysian ethnics as well. The data sets are specified based on diseases or genetic mutation types which have three main subcategories: Single Nucleotide Polymorphism (SNP), Copy Number Variation (CNV) followed by the mutations which code for the common diseases among Malaysians. MyHVPDb has been open to the local researchers, academicians and students through the registration at the portal of MyHVP (http://hvpmalaysia.kk.usm.my/mhgvc/index.php?id=register).CONCLUSIONSThis database would be useful for clinicians and researchers who are interested in doing a study on genomics population and genetic diseases in order to obtain up-to-date and accurate information regarding the population-specific variations and also useful for those in countries with similar ethnic background.

Database: Medline

16. alpha-Thalassemia with Haemoglobin Adana mutation: Prenatal diagnosis

Author(s): Zainal N.Z.; Ahmad S.; Alauddin H.; Hussin N.H.

Source: Malaysian Journal of Pathology; Dec 2014; vol. 36 (no. 3); p. 207-211

Publication Date: Dec 2014

Publication Type(s): Article

PubMedID: 25500521

Available at The Malaysian journal of pathology - from ProQuest (Health Research Premium) - NHS Version

Abstract: Thalassaemia carriers are common in the Asian region including Malaysia. Asymptomatic patients can be undiagnosed until they present for their antenatal visits. Devastating obstetric outcome may further complicate the pregnancy if both parents are thalassaemia carriers leading to hydrophic fetus due to haemoglobin Bart's disease. However in certain cases where unexplained hydrops fetalis occur in parents with heterozygous thalassaemia carrier,mutated alpha genes should be suspected. We report a twenty-nine year old woman in her third pregnancy with two previous pregnancies complicated by early neonatal death at 21 and 28 weeks of gestation due to hydrops fetalis. DNA analysis revealed the patient to have heterozygous (--SEA) alpha-gene deletion, while her husband has a compound heterozygosity for alpha3.7 deletion and codon 59 (GGC GAC) mutation of the alpha-gene. This mutation, also known as hemoglobin Adana, can explain hydrops fetalis resulting from two alpha gene deletions from the patient (mother) and a single alpha gene deletion with mutation from the father. The third pregnancy resulted in a grossly normal baby boy with 3 alpha-gene deletions (HbH disease). We postulate that, in view of heterogenisity of the alpha-thalassaemia in this patient with severely unstable haemoglobin Adana chains from her husband, there will be a 25% possibility of fetal hydrops in every pregnancy.

Database: EMBASE

17. Molecular characterization of alpha- and beta-thalassaemia among Malay patients

Author(s): Mohd Yatim N.F.; Abd. Rahim M.; Saleem M.; Yahaya B.H.; Menon K.; Al-Hassan F.M.; Ahmad R.; Manocha A.B.

Source: International Journal of Molecular Sciences; May 2014; vol. 15 (no. 5); p. 8835-8845

Publication Date: May 2014

Publication Type(s): Article

PubMedID: 24857915

Available at International Journal of Molecular Sciences - from Unpaywall

Abstract: Both alpha- and beta-thalassaemia syndromes are public health problems in the multi-ethnic population of Malaysia. To molecularly characterise the alpha- and beta-thalassaemia deletions and mutations among Malays from Penang, Gap-PCR and multiplexed amplification refractory mutation systems were used to study 13 alpha-thalassaemia determinants and 20 beta-thalassaemia mutations in 28 and 40 unrelated Malays, respectively. Four alpha-thalassaemia deletions and mutations were demonstrated. -SEA deletion and alphaCSalpha accounted for more than 70% of the alpha-thalassaemia alleles. Out of the 20 beta-thalassaemia alleles studied, nine different beta-thalassaemia mutations were identified of which betaE accounted for more than 40%. We concluded that the highest prevalence of (alpha- and beta-thalassaemia alleles in the Malays from Penang are -SEA deletion and betaE mutation, respectively.

Database: EMBASE

18. Molecular characteristic of alpha thalassaemia among patients diagnosed in UKM medical centre

Author(s): Azma R.Z.; Ainoon O.; Hafiza A.; Azlin I.; Noor Hamidah H.; Noor Farisah A.R.; Nor Hidayati S.

Source: Malaysian Journal of Pathology; Apr 2014; vol. 36 (no. 1); p. 27-32

Publication Date: Apr 2014

Publication Type(s): Article

PubMedID: 24763232

Available at The Malaysian journal of pathology - from ProQuest (Health Research Premium) - NHS Version

Abstract: Alpha (alpha) thalassaemia is the most common inherited disorder in Malaysia. The clinical severity is dependant on the number of alpha genes involved. Full blood count (FBC) and haemoglobin (Hb) analysis using either gel electrophoresis, high performance liquid chromatography (HPLC) or capillary zone electrophoresis (CE) are unable to detect definitively alpha thalassaemia carriers. Definitive diagnosis of alpha-thalassaemias requires molecular analysis and methods of detecting both common deletional and non-deletional molecular abnormailities are easily performed in any laboratory involved in molecular diagnostics. We carried out a retrospective analysis of 1623 cases referred to our laboratory in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) for the diagnosis of alpha-thalassaemia during the period October 2001 to December 2012. We examined the frequency of different types of alpha gene abnormalities and their haematologic features. Molecular diagnosis was made using a combination of multiplex polymerase reaction (PCR) and real time PCR to detect deletional and non-deletional alpha genes relevant to southeast Asian population. Genetic analysis confirmed the diagnosis of alpha-thalassaemias in 736 cases. Majority of the cases were Chinese (53.1%) followed by Malays (44.2%), and Indians (2.7%). The most common gene abnormality was alphaalpha/--SEA (64.0%) followed by alphaalpha /- alpha 3.7 (19.8%), - alpha 3.7/--SEA (6.9%), alphaalpha/alphaalpha CS (3.0%), --SEA/--SEA (1.2%), - alpha 3.7/- alpha 3.7 (1.1%), alphaalpha/-alpha4.2 (0.7%), -alpha 4.2/--SEA (0.7%), -alpha3.7/-alpha 4.2 (0.5%), alphaalpha CS/-- SEA (0.4%), alphaalpha CS/alphaalphaCd59 (0.4%), alphaalphaCS/alphaalpha CS (0.4%), -alpha3.7/alphaalpha Cd59 (0.3%), alphaalpha/alphaalphaCd59 (0.1%), alphaalpha Cd59/ alphaalphaIVS I-1 (0.1%), -alpha3.7/alphaalphaCS (0.1%) and --SEA /alphaalpha Cd59 (0.1%). This data indicates that the molecular abnormalities of alpha-thalassaemia in the Malaysian population is heterogenous. Although alpha-gene deletion is the most common cause, non-deletional alpha-gene abnormalities are not uncommon and at least 3 different mutations exist. Establishment of rapid and easy molecular techniques is important for definitive diagnosis of alpha thalassaemia, an important prerequisite for genetic counselling to prevent its deleterious complications.

Database: EMBASE

19. Severity of anemia and its obstetric implications

Author(s): Ganeshan M.; Suharjono H.; Soelar S.A.; Karalasingam S.D.; Jeganathan R.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Apr 2014; vol. 121 ; p. 156-157

Publication Date: Apr 2014

Publication Type(s): Conference Abstract

Available at BJOG: An International Journal of Obstetrics and Gynaecology - from Wiley Online Library

Abstract: Introduction Anemia is the most common medical disorder complicating a pregnancy. Despite having significant maternal and fetal implications, it remains highly prevalent. The impact of the disease is enormous, especially in developing countries. The objective of this study is to identify the obstetric implications of various severities of anemia. This will aid in identifying specific prepregnancy and therapeutic targets of treatment with the aim of preventing complications and in risk stratification of high risk group of patients. Methods This is a retrospective cohort study. The study period was from 1 January 2010 till 31 December 2012 and 119 189 pregnant mothers with anemia were studied. Specific variables were extracted from the National Obstetric Registry of Malaysia (NOR) from all the participating hospitals, which totalled to 399 274 patients. Results Anemia is highly prevalent in Malaysia with 31.5% of patients had anemia at booking. One percent of them had Thalassemia. Anemia is associated with maternal implications without any significant direct fetal implications. Even mild anemia (booking Hb >9.5 g/dL) is a significant risk factor for preterm delivery OR 1.17 (1.14-1.20, P < 0.001) and pre-eclampsia OR 1.17 (1.05-1.30, P < 0.001). Most adverse outcomes occurred for patients with haemoglobin level of between 6.5-7.9 g/dL. There is a direct correlation between severities of anemia with the severity of prematurity, up to the haemoglobin levels of 6.5 g/dL. Haemoglobin of below 6.5 g/dL is a significant risk for PPROM, OR 1.38 (0.81-2.35, P < 0.001). Haemoglobin levels of between 6.5-7.9 g/dL had an OR 1.97 (1.38-2.80, P < 0.001) to deliver below 28 weeks. The risk of pre-eclampsia was significant, OR 1.45 (0.75-2.79, P < 0.001) and is also the most significant range for having thalassemia, OR 25.78 (19.90-33.41, P < 0.001). Interestingly, anemia of various severities has no significant association with PPH, dysfunctional labour and adverse perinatal outcomes such as intrauterine growth restriction, stillbirth and birth asphyxia. Conclusion Anemia is still highly prevalent in Malaysia and requires more aggressive intervention in terms of prevention and treatment. Booking haemoglobin is an essential predictor of adverse obstetric outcomes. Booking haemoglobin should be above 11.0 g/dL to prevent preterm delivery and pre-eclampsia. The risk is highest if the haemoglobin is between 6.5 and 7.9 g/dL and Thalassemia should be excluded in such patients. Anemia is not an independent risk factor for PPH, dysfunctional labour, caesarean section, IUGR and stillbirths.

Database: EMBASE

20. Molecular basis of transfusion dependent beta-thalassemia major patients in Sabah.

Author(s): Teh, Lai Kuan; George, Elizabeth; Lai, Mei I; Tan, Jin Ai Mary Anne; Wong, Lily; Ismail, Patimah

Source: Journal of human genetics; Mar 2014; vol. 59 (no. 3); p. 119-123

Publication Date: Mar 2014

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 24369358

Available at Journal of Human Genetics - from Unpaywall

Abstract: Beta-thalassemia is one of the most prevalent inherited diseases and a public health problem in Malaysia. Malaysia is geographically divided into West and East Malaysia. In Sabah, a state in East Malaysia, there are over 1000 estimated cases of β-thalassemia major patients. Accurate population frequency data of the molecular basis of β-thalassemia major are needed for planning its control in the high-risk population of Sabah. Characterization of β-globin gene defects was done in 252 transfusion dependent β-thalassemia patients incorporating few PCR techniques. The study demonstrates that β-thalassemia mutations inherited are ethnically dependent. It is important to note that 86.9% of transfusion-dependent β-thalassemia major patients in Sabah were of the indigenous population and homozygous for a single mutation. The Filipino β(0)-deletion was a unique mutation found in the indigenous population of Sabah. Mutations common in West Malaysia were found in 11 (4.3%) patients. Four rare mutations (Hb Monroe, CD 8/9, CD 123/124/125 and IVS I-2) were also found. This study is informative on the population genetics of β-thalassemia major in Sabah.

Database: Medline

21. X-linked Charcot-Marie-Tooth disease predominates in a cohort of multiethnic Malaysian patients.

Author(s): Shahrizaila, Nortina; Samulong, Sarimah; Tey, Shelisa; Suan, Liaw Chiew; Meng, Lao Kah; Goh, Khean Jin; Ahmad-Annuar, Azlina

Source: Muscle & nerve; Feb 2014; vol. 49 (no. 2); p. 198-201

Publication Date: Feb 2014

Publication Type(s): Journal Article

PubMedID: 23649551

Available at Muscle & nerve - from Wiley Online Library

Abstract:INTRODUCTIONData regarding Charcot-Marie-Tooth disease is lacking in Southeast Asian populations. We investigated the frequency of the common genetic mutations in a multiethnic Malaysian cohort.METHODSPatients with features of Charcot-Marie-Tooth disease or hereditary liability to pressure palsies were investigated for PMP22 duplication, deletion, and point mutations and GJB1, MPZ, and MFN2 point mutations.RESULTSOver a period of 3 years, we identified 25 index patients. A genetic diagnosis was reached in 60%. The most common were point mutations in GJB1, accounting for X-linked Charcot-Marie-Tooth disease (24% of the total patient population), followed by PMP22 duplication causing Charcot-Marie-Tooth disease type 1A (20%). We also discovered 2 novel GJB1 mutations, c.521C>T (Proline174Leucine) and c.220G>A (Valine74Methionine).CONCLUSIONSX-linked Charcot-Marie-Tooth disease was found to predominate in our patient cohort. We also found a better phenotype/genotype correlation when applying a more recently recommended genetic approach to Charcot-Marie-Tooth disease.

Database: Medline

22. Distribution of alpha thalassaemia gene variants in diverse ethnic populations in malaysia: data from the institute for medical research.

Author(s): Ahmad, Rahimah; Saleem, Mohamed; Aloysious, Nisha Sabrina; Yelumalai, Punithawathy; Mohamed, Nurul; Hassan, Syahzuwan

Source: International journal of molecular sciences; Sep 2013; vol. 14 (no. 9); p. 18599-18614

Publication Date: Sep 2013

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 24025420

Abstract: Alpha thalassaemia is highly prevalent in the plural society of Malaysia and is a public health problem. Haematological and molecular data from 5016 unrelated patients referred from various hospitals to the Institute for Medical Research for α thalassaemia screening from 2007 to 2010 were retrieved. The aims of this retrospective analysis were to describe the distribution of various alpha thalassaemia alleles in different ethnic groups, along with their genotypic interactions, and to illustrate the haematological changes associated with each phenotype. Amongst the patients, 51.2% (n = 2567) were diagnosed with α thalassaemia. Of the 13 α thalassaemia determinants screened, eight different deletions and mutations were demonstrated: three double gene deletions, --(SEA), --(THAI), --(FIL); two single-gene deletions, $\alpha\text{-}^{3.7}$ and $-\alpha^{4.2}$; and three non-deletion mutations, Cd59G > A (haemoglobin [Hb] Adana), Cd125T > C (Hb Quong Sze) and Cd142 (Hb Constant Spring). A high incidence of $\alpha\text{-}^{3.7}$ deletion was observed in Malays, Indians, Sabahans, Sarawakians and Orang Asli people. However, the --SEA deletion was the most common cause of alpha thalassaemia in Chinese, followed by the $\alpha\text{-}^{3.7}$ deletion. As many as 27 genotypic interactions showed 1023 α thalassaemia silent carriers, 196 homozygous α^{+} thalassaemia traits, 973 heterozygous α^{o} thalassaemia carriers and 375 patients with Hb H disease. Statistical analysis showed a significant difference in the distribution of α thalassaemia determinants amongst the various ethnic groups. Hence, the heterogeneous distribution of common determinants indicated that the introduction of an ethnicity-targeted hierarchical α thalassaemia screening approach in this multi-ethnic Malaysian population would be effective.

Database: Medline

23. Mutational characterization of congenital adrenal hyperplasia due to 21-hydroxylase deficiency in Malaysia.

Author(s): Balraj, P; Lim, P G; Sidek, H; Wu, L L; Khoo, A S B

Source: Journal of endocrinological investigation; Jun 2013; vol. 36 (no. 6); p. 366-374

Publication Date: Jun 2013

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 23027774

Available at Journal of Endocrinological Investigation - from SpringerLink - Medicine

Abstract:BACKGROUND AND AIMCongenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD) is a common autosomal recessive disorder. Our objective was to identify the 21-hydroxylase active gene, CYP21A2 mutations in Malaysian 21-OHD patients using different techniques.MATERIALS AND METHODSBlood samples were obtained from 97 Malaysian 21-OHD patients, which included 40 siblings from 19 families. We used various techniques which include restriction enzyme digestion, Southern blot, multiple ligation-dependent probe amplification (MLPA) and sequencing to elucidate CYP21A2 mutations.RESULTSHomozygous and compound heterozygous mutations were identified in 95 of the 97 patients (98%). Deletions of CYP21A2 were found in 43 patients (44.3%). Deletions identified in CYP21A2 gene were the usual 30-kb deletion comprising 3'UTR CYP21A1P, C4B and 5'CYP21A2, complete deletion of CYP21A2 gene, deletion in exons 1-3, exons 1-6 and exons 1-8 of CYP21A2. The common mutations identified in CYP21A2 gene were deletion/conversion (22.6%), p.R356W (22%), IVS2-13A/C>G (21.3%), p.I172N (5.3%), p.Q318X (5.3%), and p.P30L (1.03%). This is the first report of the mutation frequency in CYP21A2 gene among the Malay ethnic group. Two novel mutations, c.Y97insT and p.L345P were identified in our patients. Our results show good phenotype-genotype correlation in most of the cases, although clinical variations were identified in some patients.CONCLUSIONSThe study has found various mutations including deletions in CYP21A2 gene in Malaysian patients with 21-hydroxylase deficiency using the MLPA technique that is being widely used in present laboratory settings.

Database: Medline

24. Molecular characterization of glucose-6-phosphate dehydrogenase deficiency in a university community in Malaysia

Author(s): Sulaiman A.M.; Al-Hassan F.M.; Yusoff N.M.; Zaki A.-H.A.; Saghir S.A.M.

Source: Tropical Journal of Pharmaceutical Research; Jun 2013; vol. 12 (no. 3); p. 363-367

Publication Date: Jun 2013

Publication Type(s): Article

Available at Tropical Journal of Pharmaceutical Research - from Free Medical Journals . com

Available at Tropical Journal of Pharmaceutical Research - from Unpaywall

Abstract: Purpose: To determine the prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency among staff and students of a university community in Malaysia as well as to identify molecular genetics by determination of G6PD mutations. Method(s): Cross-sectional and experimental studies were carried out on the staff and students of Advanced Medical and Dental Institute (AMDI) of Universiti Sains Malaysia (USM) from July 2009 to April 2010. Venous blood samples were collected from 87 individuals (45 males and 42 females), all of whom gave informed consent. Full blood count, reticulocyte count, screening test and quantitative determination of G6PD were performed. The deficient subjects were confirmed by standard PCR restriction enzyme. DNA samples from these subjects were analyzed for certain known G6PD mutations by digesting them with appropriate restriction enzymes. Result(s): Out of the 87 subjects (80 were Malay, 2 were Chinese, 1 was Indian and 4 were others). The total prevalence of G6PD deficiency among the subjects was 4.59% (4/87), all of whom were Malay males. One of the deficient subjects had G6PD Viangchan, while the other three were G6PD Mahidol (487 G>A). Conclusion(s): The finding of this study demonstrate that the most common mutation among AMDI staff and students is Mahidol (487G>A), followed by mutation Viangchan (871G>A).

Database: EMBASE

25. Prevalence of iron deficiency anaemia and thalassaemia trait among undergraduate medical students

Author(s): Azma R.Z.; Ainoon O.; Azlin I.; Hamenuddin H.; Hadi N.A.; Tatt W.K.; Syazana I.N.; Asmaliza A.M.; Das S.; Hamidah N.H.

Source: Clinica Terapeutica; 2012; vol. 163 (no. 4); p. 287-291

Publication Date: 2012

Publication Type(s): Article

PubMedID: 23007811

Abstract: Background. Anaemia is a global health problem including Malaysia. In adults, anaemia may affect work productivity. Iron deficiency anaemia and thalassaemia are common causes of anaemia in Malaysia. However, there is scarcity of data on national prevalence of iron deficiency anaemia and thalassaemia, especially in young adults. This cross sectional study was performed to determine the prevalence of iron deficiency anaemia and thalassaemia among medical students of Universiti Kebangsaan Malaysia Medical Centre (UKMMC). Materials and Methods. Blood samples collected in EDTA tubes were analyzed for haemoglobin level and red cell parameters such as MCV, MCH and red cell counts. Samples with abnormal red cell indices were sent for analysis of RBC morphology, iron status, haemoglobin analysis and DNA analysis. Results. A total of 400 samples were available for this study. Fiftyeight (14.5%) students had hypochromic microcytic red cell indices in which 44 (11%) showed thalassaemia red cell indices while 14 (3.5%) had iron deficiency red cell indices which were finally confirmed by serum iron/TIBC analysis. Amongst those suspected to have thalassaemia, 12

(27.3%) were confirmed as alpha thalassaemia trait (alphaalpha/--SEA), 11 (25%) as Haemoglobin-E trait, 8 (18.2%) as beta thalassaemia trait and 2 (4.5%) as Haemoglobin Constant Spring (alphaalpha/alphaCSalpha). However, eleven students (25%) with thalassaemia red cell indices could not be confirmed with the common thalassaemia primers available, thus causes have yet to be established. Conclusion. Our prevalence of thalassaemia was high and thus we opine that better screening methods should be adopted. © Societa Editrice Universo (SEU).

Database: EMBASE

26. Detection of common deletional Alpha-thalassemia spectrum by molecular technique in kelantan, northeastern Malaysia

Author(s): Rosnah B.; Rosline H.; Zaidah A.W.; Noor Haslina M.N.; Marini R.; Shafini M.Y.; Nurul Ain F.A.

Source: ISRN Hematology; 2012; vol. 2012

Publication Date: 2012

Publication Type(s): Article

Available at ISRN Hematology - from Europe PubMed Central - Open Access

Available at ISRN Hematology - from Unpaywall

Abstract: Thalassemia is a hereditary blood disorder that results from genetic defects causing deficient synthesis of hemoglobin polypeptide chains. Although thalassemia mostly affects developing countries, there is limited knowledge of its accurate frequency and distribution in these regions. Knowing the prevalence of thalassemia and the frequency of responsible mutations is therefore an important step in the prevention and control program as well as treatment strategies. This study was performed to determine the prevalence and to study the spectrum of gene deletions that are responsible in alpha-thalassemia in Kelantan, located in northeastern Malaysia. A total 400 first-time blood donors from multiple areas of donation centre were chosen randomly. The presence of three types of alpha-thalassemia gene deletion in southeast Asian population which were -SEAdeletion, -alpha3.7 rightward deletion, and -alpha4.2 leftward deletion was detected by using multiplex PCR method. 37 (9.25%) of blood donors were confirmed to have alpha-thalassemia deletion types. 34 (8%) were heterozygous for alpha3.7 deletion, 1 (0.25%) was heterozygous for 4.2 deletion, and 2 (0.5%) were heterozygous for SEA type deletion. Alpha-thalassemia-2 with 3.7 deletion was the most common determinant detected in Kelantan Malay compared to other ethnic groups. It has been noted that alpha-thalassemia-2 with 3.7 deletion is the most common type of -thalassemia throughout the world. Copyright © 2012 B. Rosnah et al.

Database: EMBASE

27. Clinical and biochemical profiles of maple syrup urine disease in malaysian children.

Author(s): Yunus, Z Md; Kamaludin, Dp Abg; Mamat, M; Choy, Y S; Ngu, Lh

Source: JIMD reports; 2012; vol. 5 ; p. 99-107

Publication Date: 2012

Publication Type(s): Journal Article

PubMedID: 23430924

Available at JIMD reports - from Unpaywall

Abstract:INTRODUCTIONMaple Syrup Urine Disease (MSUD) is an autosomal recessive disorder caused by defects in the branched-chain α-ketoacid dehydrogenase complex resulting in accumulation of branched-chain amino acids (BCAAs) and corresponding branched-chain ketoacids (BCKAs) in tissues and plasma, which are neurotoxic. Early diagnosis and subsequent nutritional modification management can reduce the morbidity and mortality. Prior to 1990s, the diagnosis of MSUD and other inborn errors of metabolism (IEM) in Malaysia were merely based on clinical suspicion and qualitative one-dimensional thin layer chromatography technique. We have successfully established specific laboratory diagnostic techniques to diagnose MSUD and other IEM. We described here our experience in performing high-risk screening for IEM in Malaysia from 1999 to 2006. We analysed the clinical and biochemical profiles of 25 patients with MSUD.METHODSA total of 12,728 plasma and urine samples from patients suspected of having IEM were received from physicians all over Malaysia. Plasma amino acids quantitation using fully automated amino acid analyzer and identification of urinary organic acids using Gas Chromatography Mass Spectrometry (GCMS). Patients' clinical information were obtained from the request forms and case records Results: Twenty-five patients were diagnosed MSUD. Nineteen patients (76%) were affected by classical MSUD, whereas six patients had non-classical MSUD. Delayed diagnosis was common among our case series, and 80% of patients had survived with treatment with mild-to-moderate learning difficulties.CONCLUSIONOur findings suggested that MSUD is not uncommon in Malaysia especially among the Malay and early laboratory diagnosis is crucial.

Database: Medline

28. Factor IX mutations in haemophilia B patients in Malaysia: a preliminary study.

Author(s): Balraj, Pauline; Ahmad, Munirah; Khoo, Alan Soo Beng; Ayob, Yasmin

Source: The Malaysian journal of pathology; Jun 2012; vol. 34 (no. 1); p. 67-69

Publication Date: Jun 2012

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 22870602

Available at The Malaysian journal of pathology - from ProQuest (Health Research Premium) - NHS Version

Abstract: Haemophilia B is caused by coagulation defects in the factor IX gene located in Xq27.1 on the X chromosome. Identification of mutations contributing to defective factor IX may be advantageous for precise carrier and prenatal diagnosis. We studied 16 patients from 11 families, consisting of 8 patients of the Malay ethnic group, of which 6 were siblings. Factor IX mutations have not been previously reported in the Malay ethnic group. The functional region of the factor IX gene was sequenced and mutations were identified in either the exon or intronic regions in 15 of the patients. One novel mutation, 6660_6664delTTCTT was identified in siblings with moderate form of haemophilia B. Mutations identified in our patients when linked with disease severity were similar to findings in other populations. In summary, this preliminary data will be used to build a Malaysian mutation database which would facilitate genetic counseling.

Database: Medline

29. Approximate Bayesian analysis of Drosophila melanogaster polymorphism data reveals a recent colonization of Southeast Asia.

Author(s): Laurent, Stefan J Y; Werzner, Annegret; Excoffier, Laurent; Stephan, Wolfgang

Source: Molecular biology and evolution; Jul 2011; vol. 28 (no. 7); p. 2041-2051

Publication Date: Jul 2011

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 21300986

Available at Molecular biology and evolution - from Oxford Journals - Medicine

Abstract: Southeast Asian populations of the fruit fly Drosophila melanogaster differ from ancestral African and derived European populations by several morphological characteristics. It has been argued that this morphological differentiation could be the result of an early colonization of Southeast Asia that predated the migration of D. melanogaster to Europe after the last glacial period (around 10,000 years ago). To investigate the colonization process of Southeast Asia, we collected nucleotide polymorphism data for more than 200 X-linked fragments and 50 autosomal loci from a population of Malaysia. We analyzed this new single nucleotide polymorphism data set jointly with already existing data from an African and a European population by employing an Approximate Bayesian Computation approach. By contrasting different demographic models of these three populations, we do not find any evidence for an early divergence between the African and the Asian populations. Rather, we show that Asian and European populations of D. melanogaster share a non-African most recent common ancestor that existed about 2,500 years ago.

Database: Medline

30. Berend houwen memorial lecture - New insights into thalassemia and hemoglobinopathies

Author(s): Fucharoen S.; Winichagoon P.

Source: International Journal of Laboratory Hematology; May 2011; vol. 33 ; p. 4-5

Publication Date: May 2011

Publication Type(s): Conference Abstract

Available at International Journal of Laboratory Hematology - from Wiley Online Library

Abstract: Thalassemia is a group of common genetic diseases that reaches its highest frequency in Asian countries. It affects children from birth, leading to long lasting suffering, impedes productivity among those who live to adulthood and causes premature death. Beta-thalassemia and Hb Constant Spring (Hb CS) are prevalent throughout the region at 1-8%. Hb E is found in the eastern half of the Indian Subcontinent and throughout Southeast (SE) Asia, especially at the junction of Cambodia, Laos and Thailand where the prevalence reaches 50-60%. Hb E is also common in certain ethnic group in Indonesia, Malaysia, Vietnam and south China. Alpha-thalassemia has a focus in the northeastern part of SE Asia around Laos and Thailand at frequencies of 30-40%. The complex gene-gene interactions lead to many thalassemic diseases including homozygous betathalassemia, beta-thalassemia/Hb E and Hb Bart's hydrops fetalis. It has been estimated that the conception of homozygous beta-thalassemia and beta-thalassemia/Hb E in Asia is 0.24 and 0.25 per 1000 births, respectively. Thousands of patients with beta-thalassemia disorders are living in Asia. The prevention and control of thalassemia consist of two strategic plans, the first is to offer the best treatment to patients and second is to prevent the birth of new cases. The initial screening for thalassemia measures the MCV and MCH using an electronic cell counter. Thresholds below which

the likelihood of some form of thalassemia is high are well established. The diagnosis of beta-thalassemia is confirmed by finding a raised level of Hb A2 using chromatography or quantitative hemoglobin electrophoresis. High-performance liquid chromatography (HPLC) and capillary electrophoresis (CE) have been recently used for easy and accurate Hb A2 measurement. However, the HPLC and CE hardware is expensive and the cost per sample is more than US$ 7-8 and therefore several more economical approaches have been developed. The initial screening can be done using a single-tube osmotic fragility test, which even though it may result in a relatively high number of false positive results from iron deficiency anemia, it usually gives few false negatives. Commercial kits for osmotic fragility testing have recently been introduced and validated in Thailand. A simple stability test for unstable hemoglobin like Hb E has also been developed and is used as primary screening tool in the rural areas where facilities are limited. Almost all thalassemia patients with anemia receive regular blood transfusion and end up with different degrees of organ damage from iron overload. Desferrioxamine is the only injectable iron chelator available since 1960. As an alternative to desferrioxamine, oral iron chelators have been developed during the last 20 years. Deferiprone and deferasirox are two oral iron chelators being used worldwide with good compliance bringing better quality of life to thalassemia patients. The only cure for thalassemia is by stem cell transplantation, and the first case of successful gene therapy was recently reported. The stimulation of Hb F production and Hb switching is still enlarging investigation. While there has been significant progress in improving the quality of life of thalassemia patients, the cost of these treatments are still too high in nations with limited resources. The only long term solution to handle the problem of thalassemia is to prevent the birth of new cases, a policy that has been shown to have succeeded in some Mediterranean countries. In theory, premarital screening for thalassemia is a standard practice and most at-risk couples are identified early for prenatal diagnosis in the first pregnancy and the majority use this service and produce healthy offspring. Thalassemia carriers are detected mainly through the expanded family study of cases with thalassemic diseases. Prevention of thalassemia is progressing in many developing countries with the announcement of national control programs. The increasing problem of thalassemia and sickle cell anemia were recognized by the WHO and reported in Genomics and World Health (2002). Among the recommendations of the report it was suggested that for more effective control and management of thalassemia the principle of the further development of North/South partnerships should be pursued and that the possibility of South/South networks should also be examined. International collaboration including technology transfer, manpower and infrastructure development is needed to support countries that do not have experience and limited resource. In 2004 representatives from a number of Asian countries together with workers in the thalassemia field from the UK, Canada and Australia decided to work together towards the prevention and control of thalassemia in Asia. It was agreed that the Network should focus on fact finding regarding the extent of the problem in individual countries together with an accounting of the facilities that exist for the diagnosis and management of the different forms of thalassemia in each country. The health burden of the thalassemias in Asia should be translated into disability adjusted life years (DALYs). Using this approach it is possible to compare the health burden of the thalassemias with other health problems in Asia. Although the preliminary data indicate that thalassemia poses a health burden comparable with some of the major communicable diseases, far more data are required, particularly regarding gene frequency and an accurate costing of both prevention and treatment regimes.

Database: EMBASE

31. Prevalence and molecular study of G6PD deficiency in Malaysian Orang Asli

Author(s): Amini F.; Ismail E.; Zilfalil B.-A.

Source: Internal Medicine Journal; Apr 2011; vol. 41 (no. 4); p. 351-353

Publication Date: Apr 2011

Publication Type(s): Article

PubMedID: 21507164

Available at Internal medicine journal - from Wiley Online Library

Abstract: This study aims to define the prevalence and the molecular basis of G6PD deficiency in the Negrito tribe of the Malaysian Orang Asli. Four hundred and eighty seven consenting Negrito volunteers were screened for G6PD deficiency through the use of a fluorescent spot test. DNA from deficient individuals underwent PCR-RFLP analysis using thirteen recognized G6PD mutations. In the instances when the mutation could not be identified by PCR-RFLP, the entire coding region of the G6PD gene was subjected to DNA sequencing. In total, 9% (44/486) of the sample were found to be G6PD-deficient. However, only 25 samples were subjected to PCR-RFLP and DNA sequencing. Of these, three were found to carry Viangchan, one Coimbra and 16, a combination of C1311T in exon 11 and IVS11 T93C. Mutation(s) for the five remaining samples are unknown. The mean G6PD enzyme activity ranged 5.7IU/gHb in deficient individuals. Our results demonstrate that the frequency of G6PD deficiency is higher among the Negrito Orang Asli than other Malaysian races. The dual presence of C1311T and IVS11 T93C in 64% of the deficient individuals (16/44) could well be a result of genetic drift within this isolated group. © 2011 The Authors. Internal Medicine Journal © 2011 Royal Australasian College of Physicians.

Database: EMBASE

32. High prevalence of alpha- and beta-thalassemia in the kadazandusuns in east Malaysia: Challenges in providing effective health care for an indigenous group

Author(s): Tan J.-A.M.A.; Wee Y.-C.; Tan K.-L.; Mahali N.F.; Chua K.-H.; Lee P.-C.; George E.

Source: Journal of Biomedicine and Biotechnology; 2010; vol. 2010

Publication Date: 2010

Publication Type(s): Article

PubMedID: 20871816

Available at Journal of Biomedicine and Biotechnology - from Europe PubMed Central - Open Access

Available at Journal of Biomedicine and Biotechnology - from Free Medical Journals . com

Available at Journal of Biomedicine and Biotechnology - from Unpaywall

Abstract: Thalassemia can lead to severe transfusion-dependent anemia, and it is the most common genetic disorder in Malaysia. This paper aims to determine the prevalence of thalassemia in the Kadazandusuns, the largest indigenous group in Sabah, East Malaysia. - and -thalassemia were confirmed in 33.6 and 12.8, of the individuals studied respectively. The high prevalence of - and -thalassemia in the Kadazandusuns indicates that thalassemia screening, genetic counseling, and prenatal diagnosis should be included as part of their healthcare system. This preliminary paper serves as a baseline for further investigations into the health and genetic defects of the major indigenous population in Sabah, East Malaysia. © 2010 Jin-Ai Mary Anne Tan et al.

Database: EMBASE

33. Genotype-phenotype diversity of beta-thalassemia in Malaysia: treatment options and emerging therapies.

Author(s): George, Elizabeth; Ann, T J A Mary

Source: The Medical journal of Malaysia; Dec 2010; vol. 65 (no. 4); p. 256-260

Publication Date: Dec 2010

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 21901940

Abstract: The haemoglobinopathies and thalassemias represent the most common inherited monogenic disorders in the world. Beta-thalassaemia major is an ongoing public health problem in Malaysia. Prior to 2004, the country had no national policy for screening and registry for thalassemia. In the absence of a national audit, the true figure of the extent of thalassemia in the Malaysian population was largely presumptive from micro-mapping studies from various research workers in the country. The estimated carrier rate for beta-thalassemia in Malaysia is 3.5-4%. There were 4768 transfusion dependent thalassemia major patients as of May 2010 (Data from National Thalassemia Registry).

Database: Medline

34. Birth defects, the challenges ahead for Malaysia

Author(s): Boo N.Y.

Source: Medical Journal of Malaysia; 2005; vol. 60 (no. 4); p. 404-406

Publication Date: 2005

Publication Type(s): Editorial

Database: EMBASE

35. Characterisation of beta-globin gene mutations in Malaysian children: a strategy for the control of beta-thalassaemia in a developing country.

Author(s): Thong, Meow-Keong; Tan, J A M A; Tan, K L; Yap, S F

Source: Journal of tropical pediatrics; Dec 2005; vol. 51 (no. 6); p. 328-333

Publication Date: Dec 2005

Publication Type(s): Journal Article

PubMedID: 15967770

Available at Journal of Tropical Pediatrics - from Oxford Journals - Medicine

Abstract:beta-thalassaemia major, an autosomal recessive hemoglobinopathy, is one of the most common single gene disorders in multi-racial Malaysia. The control of beta-thalassaemia major requires a multi-disciplinary approach that includes population screening, genetic counselling, prenatal diagnosis and the option of termination of affected pregnancies. To achieve this objective, the molecular characterisation of the spectrum of beta-globin gene mutations in each of the affected ethnic groups is required. We studied 88 consecutive unrelated individuals and their respective families with beta-thalassaemia (74 beta-thalassaemia major, 12 HbE-beta-thalassaemia, 2 with HbE homozygotes) and four individuals with beta-thalassaemia trait that contributed a total 180 alleles for study. Using a 2-step molecular diagnostic strategy consisting of amplification refractory mutation system (ARMS) to identify the 8 most common mutations followed by other DNA-based diagnostic techniques, a total of 177 (98.3 per cent) of the 180 beta-thalassaemia alleles

were characterised. One out of 91 (1 per cent) of the Chinese alleles, one out of 46 (2.2 per cent) Malay alleles and one out of two Indian alleles remained unknown. A 100 per cent success rate was achieved in studying the Kadazandusun community in this study. A strategy to identify beta-globin gene mutations in Malaysians with beta-thalassaemia is proposed based on this outcome.

Database: Medline

36. Heterogeneity in alpha-thalassemia interactions in Malays, Chinese and Indians in Malaysia.

Author(s): Wee, Yong-Chui; Tan, Kim-Lian; Chow, Teresa Wai-Ping; Yap, Sook-Fan; Tan, Jin-Ai Mary Anne

Source: The journal of obstetrics and gynaecology research; Dec 2005; vol. 31 (no. 6); p. 540-546

Publication Date: Dec 2005

Publication Type(s): Research Support, Non-u.s. Gov't Comparative Study Journal Article

PubMedID: 16343256

Available at Journal of Obstetrics and Gynaecology Research - from Wiley Online Library

Abstract:AIMInteractions between different determinants of alpha-thalassemia raises considerable problems, particularly during pregnancies where antenatal diagnosis is necessary. This study aims to determine the different types of deletional alpha-thalassemia and Hemoglobin Constant Spring (HbCS), and their frequency in Malays, Chinese and Indians in Malaysia.METHODSDNA from 650 pregnant women from the Antenatal Clinic of the University of Malaya Medical Center in Kuala Lumpur, Malaysia who showed mean cell volume < or =89 fL and/or mean cell hemoglobin < or =28 pg were analyzed for the double alpha-globin gene South-East Asian deletion (--SEA), the -alpha3.7 and -alpha4.2 single alpha-globin gene deletions and HbCS.RESULTSOne hundred and three (15.8%) of the pregnant women were confirmed as alpha-thalassemia carriers: 25 (3.8%) were alpha-thalassemia-1 carriers with the --SEA/alphaalpha genotype, 64 (9.8%) were heterozygous for the -alpha3.7 rightward deletion (-alpha3.7/alphaalpha), four (0.6%) were heterozygous for the -alpha4.2 leftward deletion (-alpha4.2/alphaalpha), nine (1.4%) were heterozygous for HbCS (alphaCSalpha/alphaalpha) and one (0.2%) was compound heterozygous with the -alpha3.7/alphaCSalpha genotype. The double alpha-globin gene --SEA deletion was significantly higher in the Chinese (15%) compared to the Malays (2.5%) and not detected in the Indians studied. The -alpha3.7 deletion was distributed equally in the three races. HbCS and -alpha4.2 was observed only in the Malays.CONCLUSIONThe data obtained gives a better understanding of the interactions of the different alpha-thalassemia determinants in the different ethnic groups, thus enabling more rapid and specific confirmation of alpha-thalassemia in affected pregnancies where antenatal diagnosis is necessary.

Database: Medline

37. Audit of birth defects in 34,109 deliveries in a tertiary referral center

Author(s): Noraihan M.N.; See M.H.; Raja R.; Baskaran T.P.; Symonds E.M.

Source: The Medical journal of Malaysia; Oct 2005; vol. 60 (no. 4); p. 460-468

Publication Date: Oct 2005

Publication Type(s): Article

PubMedID: 16570708

Abstract: The objective of the study is to determine the proportion and different types of birth defects among the children born in Hospital Kuala Lumpur. A cross-sectional study was conducted for a period of 18 months where all consecutively born infants, dead or alive were included. There were total of 34,109 births recorded during this period. The proportion of birth defects in Hospital Kuala Lumpur was 3.1% (n = 1056). The commonest involved were the hematology system, (157.7 per 10,000 births), the central nervous system, genitourinary system and chromosomal anomalies. The proportion was significantly higher in males and in the Chinese ($p < 0.001$). The commonest abnormalities are Glucose 6 Phosphate Deficiency (157.7/10000), Down's syndrome (12.6/10000), thalassaemia (8.8/10000), cleft lip and/or palate (7.6/10000) and anencephaly (7.3/10000). Neural tube defect is common and ranked second after G6PD deficiency. There is a need for a birth defect registry to assess the extent of the problem in Malaysia.

Database: EMBASE

38. The spectrum of beta-globin gene mutations in children with beta-thalassaemia major from Kota Kinabalu, Sabah, Malaysia.

Author(s): Thong, M K; Soo, T L

Source: Singapore medical journal; Jul 2005; vol. 46 (no. 7); p. 340-343

Publication Date: Jul 2005

Publication Type(s): Journal Article

PubMedID: 15968446

Abstract:INTRODUCTIONBeta-thalassaemia major is one of the commonest genetic disorders in South East Asia. The strategy for the community control of beta-thalassaemia major requires the characterisation of the spectrum of beta-globin gene mutations in any multi-ethnic population. There is only a single report of mutation analyses of the beta-globin gene in an isolated Kadazandusun community in Kota Belud, Sabah, Malaysia, which showed the presence of a common 45 kb deletion.METHODSTo confirm the observation that this large deletion is the commonest beta-globin gene mutation among the Kadazandusun and other indigenous populations in Sabah, Malaysia, we performed polymerase chain reaction (PCR) analysis of the beta-globin gene in ten children with beta-thalassaemia major attending the Thalassaemia Centre, Queen Elizabeth Hospital, the major paediatric referral centre in Kota Kinabalu, Sabah.RESULTSThe 45 kb deletion was confirmed to be the commonest mutation found in the Kadazandusun, Bajau and Murut populations, whereby it was detected in 19 out of the 20 (95 percent) alleles analysed. The other mutation was due to an IVS-1 position 1 G > T mutation.CONCLUSIONThis finding confirmed the deletion in the homozygous state was associated with a severe phenotype. The reason for the predominance of this mutation in Kota Kinabalu is most likely to be due to founder effects and possibly intermarriages between the various ethnic groups. Prenatal diagnosis using PCR for this common mutation is feasible in this community. Medical workers and scientists at molecular diagnostic centres serving large South East Asian populations should incorporate a diagnostic strategy for this deletion in the appropriate population. Future studies on these indigenous ethnic groups in other areas and other groups in Sabah are required.

Database: Medline

39. Diagnosis and management of Duchenne muscular dystrophy in a developing country over a 10-year period

Author(s): Thong M.-K.; Bazlin R.I.R.; Wong K.-T.

Source: Developmental Medicine and Child Neurology; Jul 2005; vol. 47 (no. 7); p. 474-477

Publication Date: Jul 2005

Publication Type(s): Article

PubMedID: 15991868

Abstract: Clinical data on Duchenne muscular dystrophy (DMD) are lacking in developing countries. The objective of this study was to delineate the demographic characteristics, investigations, and outcome of 21 Malaysian males diagnosed with DMD over a period of 10 years. Mean age presentation was 3 years 8 months (SD 23mo; range 10 to 84mo), mean duration from first presentation to diagnosis was 3y 7mo (SD 26mo; range 5 to 84) and the mean age for loss of ambulation was 11 years (SD 25mo; range 102 to 168). There was family history of DMD in five of the 21 patients. Muscle biopsy showed confirmatory findings of DMD in the 16 patients tested. Molecular genetic analysis showed dystrophin gene deletions in 11 of these 16 patients. Four and seven of the students stopped schooling and had learning difficulties, respectively; only nine had satisfactory school performances. Eight out of 14 patients evaluated were classified as having severe to total dependency levels on the modified Barthel Index for activities of daily living assessment. DMD is associated with significant medical and social needs for a developing country such as Malaysia. Earlier referral, genetic counselling, and provision of support and rehabilitative services are the main priorities.

Database: EMBASE

40. Molecular defects in the beta-globin gene identified in different ethnic groups/populations during prenatal diagnosis for beta-thalassemia: A Malaysian experience

Author(s): Tan J.A.M.A.; Tan K.L.; George E.; Chow T.; Tan P.C.; Hassan J.; Chia P.; Subramanium R.; Chandran R.; Yap S.F.

Source: Clinical and Experimental Medicine; Apr 2004; vol. 4 (no. 3); p. 142-147

Publication Date: Apr 2004

Publication Type(s): Article

PubMedID: 15599663

Available at Clinical and experimental medicine - from SpringerLink - Medicine

Available at Clinical and experimental medicine - from ProQuest (Health Research Premium) - NHS Version

Abstract:beta-thalassemia is the most-common genetic disorder of hemoglobin synthesis in Malaysia, and about 4.5% of the population are heterozygous carriers of the disorder. Prenatal diagnosis was performed for 96 couples using the Amplification Refractory Mutation System and Gap-Polymerase Chain Reaction. We identified 17 beta-globin defects-initiation codon for translation (T-G), -29 (A-G), - 28 (A-G), CAP +1 (A-C), CD 8/9 (+G), CD 15 (G-A), CD 17 (A-T), CD 19 (A-G), Hb E (G-A), IVS1-1 (G-T), IVS1-5 (G-C), CD 41/42 (-CTTT), CD 71-72 (+A), IVS2-654 (C-T), poly A (A-G), 100-kb Ggamma(Agammadeltabeta)degree and 45-kb Filipino deletions. The 192 beta-alleles studied comprised Chinese (151 patients), Malay (21), Orang Asli from East Malaysia (15), Filipino (1), Indian (1), Indonesian Chinese (2), and Thai (1). In the Chinese, 2 beta-globin defects at CD 41/42 and IVS2-654 were responsible for 74% of beta-thalassemia. beta-mutations at CD 19, IVS1-1 (G-T), IVS1-5, poly A, and hemoglobin E caused 76% of the hemoglobin disorders in the Malays. The Filipino 45-kb deletion caused 73.3% of b-thalassemia in the Orang Asli. Using genomic sequencing, the rare Chinese beta-mutation at CD 43 (G-T) was confirmed in 2 Chinese, and the Mediterranean mutation IVS1-1 (G-A) was observed in a Malay beta-thalassemia carrier. The beta-globin mutations confirmed in this prenatal diagnosis study were heterogenous and 65 (68%) couples showed a different globin defect from each other. The use of specific molecular protocols has allowed rapid and successful prenatal diagnosis of beta-thalassemia in Malaysia.

Database: EMBASE

41. Glucose-6-phosphate dehydrogenase (G6PD) variants in Malaysian Malays

Author(s): Ainoon O.; Yu Y.H.; Amir Muhriz A.L.; Boo N.Y.; Cheong S.K.; Hamidah N.H.

Source: Human mutation; Jan 2003; vol. 21 (no. 1); p. 101

Publication Date: Jan 2003

Publication Type(s): Article

PubMedID: 12497642

Available at Human Mutation - from Wiley Online Library

Available at Human Mutation - from ProQuest (Health Research Premium) - NHS Version

Abstract: We performed DNA analysis using cord blood samples on 86 male Malay neonates diagnosed as G6PD deficiency in the National University of Malaysia Hospital by a combination of rapid PCR-based techniques, single-stranded conformation polymorphism analysis (SSCP) and DNA sequencing. We found 37.2% were 871G>A (G6PD Viangchan), 26.7% were nt 563 C>T (G6PD Mediterranean) and 15.1% were 487G>A (G6PD Mahidol) followed by 4.7% 1376G>T (G6PD Canton), 3.5% 383T>C (G6PD Vanua Lava), 3.5% 592C>T (G6PD Coimbra), 2.3% 1388G>A (G6PD Kaiping), 2.3% 1360C>T (G6PD Union), 2.3% 1003G>A (G6PD Chatham), 1.2% 131C>G (G6PD Orissa) and 1.2%

1361G>A (G6PD Andalus). Seventy-one (82.6%) of the 86 G6PD-deficient neonates had neonatal jaundice. Fifty seven (80%) of the 71 neonates with jaundice required phototherapy with only one neonate progressing to severe hyperbilirubinemia (serum bilirubin >340 micromol/l) requiring exchange transfusion. There was no significant difference in the incidence of neonatal jaundice, mean serum bilirubin level, mean age for peak serum bilirubin, percentage of babies requiring phototherapy and mean number of days of phototherapy between the three common variants. In conclusion, the molecular defects of Malay G6PD deficiency is heterogeneous and G6PD Viangchan, Mahidol and Mediterranean account for at least 80% of the cases. Our findings support the observation that G6PD Viangchan and Mahidol are common Southeast Asian variants. Their presence in the Malays suggests a common ancestral origin with the Cambodians, Laotians and Thais. Our findings together with other preliminary data on the presence of the Mediterranean variant in this region provide evidence of strong Arab influence in the Malay Archipelago. Copyright 2002 Wiley-Liss, Inc.

Database: EMBASE

42. Molecular heterogeneity of glucose-6-phosphate dehydrogenase deficiency in Malays in Malaysia.

Author(s): Yusoff, Narazah Mohd; Shirakawa, Taku; Nishiyama, Kaoru; Ghazali, Selamah; Ee, Choo Keng; Orita, Ayako; Abdullah, Wan Zaidah; Isa, Mohd Nizam; Van Rostenberghe, Hans; Matsuo, Masafumi

Source: International journal of hematology; Aug 2002; vol. 76 (no. 2); p. 149-152

Publication Date: Aug 2002

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 12215013

Available at International journal of hematology - from SpringerLink - Medicine

Available at International journal of hematology - from ProQuest (Health Research Premium) - NHS Version

Abstract: Multiplex polymerase chain reaction (PCR) using multiple tandem forward primers and a common reverse primer (MPTP) was recently established as a comprehensive screening method for mutations in X-linked recessive diseases. In the work reported here, MPTP was used to scan for mutations of the glucose-6-phosphate dehydrogenase (G6PD) gene. Mutations in exons 3,4,5,6,7,9, 11, and 12 of the G6PD gene were screened by MPTP in 93 unrelated Malaysian patients with G6PD deficiency. Of the 93 patients, 80 (86%) had identified mutations. Although all of these were missense mutations, identified nucleotide changes were heterogeneous, with 9 mutations involving various parts of the exons. These 9 mutations were G-to-A nucleotide changes at nucleotide 871 of the G6PD gene (G871A), corresponding to G6PD Viangchan, G6PD Mediterranean (C563T), G6PD Vanua Lava (T383C), G6PD Coimbra (C592T), G6PD Kaiping (G1388A), G6PD Orissa (C131G), G6PD Mahidol (G487A), G6PD Canton (G1376T), and G6PD Chatham (G1003A). Our results document heterogeneous mutations of the G6PD gene in the Malaysian population.

Database: Medline

Strategy 793959

#	Database	Search term	Results
1	EMBASE	exp "AUTOSOMAL RECESSIVE DISORDER"/	177865
2	EMBASE	("autosomal recessive" ADJ2 (disease* OR disorder*)).ti,ab	21083
3	EMBASE	(1 OR 2)	185923
4	EMBASE	(Malaysia OR Malaysian*).ti,ab	24305
5	EMBASE	exp MALAYSIAN/	1699
6	EMBASE	exp MALAYSIA/	21180
7	EMBASE	(4 OR 5)	24663
8	EMBASE	(3 AND 7)	273
9	Medline	("autosomal recessive" ADJ2 (disease* OR disorder*)).ti,ab	16548
10	Medline	exp THALASSEMIA/	22481
11	Medline	(thalassemia*).ti,ab	16041
12	Medline	(9 OR 10 OR 11)	43100
13	Medline	(Malaysia OR Malaysian*).ti,ab	17748
14	Medline	(12 AND 13)	139
15	Medline	(malay).ti,ab	3392
16	Medline	(12 AND 15)	75
17	EMBASE	exp THALASSEMIA/	32012
18	EMBASE	(7 AND 17)	187
19	EMBASE	*"GENETIC DISORDER"/	17478

20	EMBASE	(7 AND 19)	10
21	Medline	exp "GENETIC DISEASES, INBORN"/	687696
22	Medline	(13 AND 21)	333
23	Medline	exp MALAYSIA/	14455
24	Medline	(9 AND 23)	11
25	Medline	(10 AND 23)	103
26	Medline	("x linked").ti,ab	28449
27	Medline	exp "GENETIC DISEASES, X-LINKED"/	42048
28	Medline	(26 OR 27)	62247
29	Medline	(23 AND 28)	23
30	Medline	(13 AND 28)	27
31	Medline	(29 OR 30)	31
32	EMBASE	("x linked").ti,ab	37284
33	EMBASE	exp "X CHROMOSOME LINKED DISORDER"/	99690
34	EMBASE	(32 OR 33)	121724
35	EMBASE	(7 AND 34)	103
36	EMBASE	exp "GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY"/	4633
37	EMBASE	(7 AND 36)	36
38	Medline	exp "GLUCOSEPHOSPHATE DEHYDROGENASE DEFICIENCY"/	4967

39	Medline	(23 AND 38)	35