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P113 INCIDENCE OF HAEMOGLOBINOPATHY IN SLOVAKIA

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Background: The paper presents results of 27- year epidemiological study of screening and follow-up haemoglobinopathies in Slovakia.
Aims: The incidence of haemoglobinopathies in Slovek Republic
Methods: Between 1993 – 2020, in two centres in Bratislava and in one centre in Kosice, carriers of beta-thalassaemic genes or other haemoglobinopathies were searched for. Patients with a probability of having a haemoglobinopathy were sent to the research facilities. Diagnosis was performed by haematologists, whereby the family history was evaluated, together with overall clinical condition, blood count and blood smear, iron and haemolysis parameters, mutations of hereditary haemochromatosis, and haemoglobin electrophoresis testing.
Results: A clinical suspicion of the heterozygous form of beta-thalassaemia or other haemoglobinopathies was documented in 694 patients. Of them 25 (6.04%) patients were foreigners. 415 (59.85%) patients were genetically examined. In 385 (92.99%) of them heterozygote beta-thalassaemia was confirmed (in 98 families). Five patients (1.21%) were diagnosed for delta,beta-thalassaemia, 4 patients (0,97%) for delta,beta-gama1-thalasaemia or persistent hereditary fetal haemoglobin. In total we diagnosed 20 mutations of beta-globin gene. The most frequent mutations were IVS 1.110 (G-A), IVS II-1(G-A) and codon 39. Evidence of haemoglobin S (heterozygote sickle cell anaemia) was also notable in two non-relative children, whose fathers were of African origin, in one patient of Ghana and in one patient from Nigeria. One female patient was followed up for haemoglobin Santa Ana (mutation de novo), one family for haemoglobin Bishopstown and one patient for mutation KLF1 gene.
In our group were 14 patients (3.14%) diagnosed for alpha-thalassaemia. All patients were heterozygotes, only one female patient from Macedonia was a double heterozygote for beta-thalasaemie. Clinicaly all of the patients had a minor or intermedia form. In the years of 2012–2019 we observed 12 pregnant patients with beta-thalasaemie. One of them had multiple pregnancies, all deliveries were without haematological complications.
Conclusions: The study showed that in the west and eastern Slovakia there is a higher number for thalassaemia and other haemoglobinopathies. Mutations are of historical origin or over the past years we have recorded an increase number of mutations from areas with high incidence of haemoglobinopathies. It is necessary to continue in search of pathological gene carriers to avoid serious forms of the disease.
Key words: thalassaemia – sickle cell disease – prevention- epidemiological study – Slovakia

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P114 NEWBORN SCREENING FOR HAEMOGLOBINOPATHIES IN BIDA, NORTH CENTRAL NIGERIA.

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Background: The global annual population of newborns with structural haemoglobin disorders is estimated at five million. Nigeria accounts for more than 30% of these in Sub-Saharan Africa with under-five mortality from haemoglobinopathies reaching 50–90%. Despite this huge burden and a 15-fold reduction in deaths from haemoglobinopathies in countries that conduct newborn screening, most sub-Saharan Africa countries do not have a screening program. Haemoglobin electrophoresis is also not sensitive for newborn screening.
Objectives: This study was carried out to determine haemoglobin phenotype patterns and frequency in neonates attending routine immunization clinics in Bida, and to identify factors associated with the occurrence of haemoglobinopathy.
Methods: It was a descriptive cross-sectional study that recruited 254 neonates by multi-staged sampling technique from nine immunisation centres. Heel prick blood sample collected on Guthrie cards were tested using High-Performance Liquid Chromatography (HPLC). The relationship of various risk factors with the occurrence of an abnormal haemoglobin variant was analysed with the Statistical Package for Social Sciences.
Results: The Hb phenotypes found in this study were HbFA- 73.6% (187/254), HbFAS- 23.2% (59/254), HbFAC- 1.6% (4/254), HbFS- 1.2% (3/254), and HbFAD-0.4% (1/254). There was an almost equal abnormal haemoglobin occurrence in both genders. The majority (89%) of mothers did not know their Hb phenotype, one-quarter of these had a newborn with an abnormal phenotype and 20% married in consanguineous marriages. Wrong perception of sickle cell disease was common.
Conclusion: Abnormal haemoglobin variants were present in more than one-quarter (26.4%) of the neonatal population studied in Bida. Most parents were not aware of their haemoglobin phenotype and had a wrong perception of sickle cell disease. Consanguinity though common in the population did not significantly affect the occurrence of an abnormal haemoglobin phenotype.

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P115 REAL-WORLD DATA ON THE EFFICACY OF PHARMACEUTICAL-GRADE L-GLUTAMINE IN PREVENTING SICKLE CELL DISEASE-RELATED ACUTE COMPLICATIONS AND HEMOLYSIS IN PEDIATRIC AND ADULT PATIENTS.

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Background: Oxidative stress is a key contributors to the pathophysiology of sickle cell disease (SCD) and related complications including acute pain (vaso-occlusive crisis VOC) and acute chest syndrome (ACS) [1, 2]. L-glutamine (L-Gln), a precursor of nicotinamide adenine dinucleotide (NAD), has been shown to play a key role in the regulation of oxidative stress[3]. In a pivotal Phase 3 trial, L-Gln demonstrated significant

reduction in VOCs, hospitalizations, and ACS events compared to placebo in patients with SCD, with or without hydroxyurea (HU) use, over a 48-week period [4]. In September 2021, a re-analysis of the trial data revealed that L-Gln decreased the number of VOCs by 45% [5].
Aims: To confirm the efficacy of pharmaceutical-grade L-glutamine in pediatric and adult patients with SCD at follow-up time points of 24, 48 and 72 weeks.
Methods: In a retrospective study conducted from October 2019 to April 2020, 19 patients (4 patients from Qatar and 15 patients from French Guyana) were treated orally with L-Gln (0.3mg/kg) twice daily. Laboratory parameters (hemoglobin levels (Hg), hematocrit proportion (Ht), WBC counts, reticulocyte counts, and LDH levels) were measured at baseline and follow-up time points. Clinical parameters (number of VOCs, hospitalizations, days hospitalized, ACS events, and blood transfusions) were documented for the year prior to treatment initiation as baseline values. These parameters were also collected at 24, 48, and 72 weeks from treatment initiation. Adverse events (AEs) were also collected during the treatment period. The data values at 24, 48, and 72 weeks have been annualized. Statistical analysis was performed using MedCalc Version 20.015.
Results: 19 patients (HbSS, age range, 8–54 years; 53% patients <18 years) were retrospectively analyzed. 63% of the patients were receiving HU at baseline and 47% received concomitant HU during the study. Compared to baseline, patients had significantly fewer VOCs at 24, 48, and 72 weeks following L-Gln therapy (median change from 3.0 to 0; P<0.00001). Compared to baseline, there were fewer hospitalizations (median change from 3.0 to 0; P<0.00001) and patients spent fewer days in hospital (median change from 15.0 to 0; P<0.00001). Moreover, at 24, 48, and 72 weeks, the number of blood transfusions was considerably lower than at baseline (median, from 3.0 to 0; P<0.00001). In the year prior to treatment initiation, 2 patients reported a single ACS event, but, no such events were observed during therapy. Following treatment with L-Gln, the mean Hg level increased significantly from baseline to 72 weeks (8.2 to 8.8 g/dL; P<0.001) with peak mean increase from baseline of 11.2% at 48 weeks. A similar increasing trend was observed for Ht from baseline to 72 weeks (24% to 27%; P<0.001) with highest mean improvement from baseline of 15.5% at 48 weeks. Conversely, mean reticulocyte counts and LDH levels were significantly reduced at follow-up time points compared to baseline (P=0.003 and P<0.001, respectively). Only few AEs occurred and were mild. No compliance issue was reported.
Conclusions: This study demonstrated that L-Gln therapy in SCD patients from Qatar and French Guyana resulted in significant and sustained improvements in clinical outcomes (number of VOCs, number and duration of hospitalizations, and number of blood transfusions) and an increase in Hg and a reduction of hemolysis. 2 patients with a history of ACS did not experience any of those events during L-Gln therapy.

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P116 THE IMPACT OF COVID19 PANDEMIC ON SICKLE CELL MANAGEMENT: EXPERIENCE OF A SINGLE PEDIATRIC CENTER

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Background: COVID19 pandemic has put an incomparable pressure on all health services – including those offered to hemoglobinopathy patients. Sickle cell disease management, although not routinely requiring inpatient facilities, is dependent upon hospital based services on a great extent.
Aims: Aim of the present study was to evaluate the impact of COVID19 pandemic on medical management of sickle cell disease patients followed at a single pediatric center in Northern Greece.
Methods: Patient records were reviewed in order to assess changes reflecting limited access to specialized care, i.e. number of disease related complications, number of hospital routine visits and number of disease related hospitalizations, during the 18month pandemic in Greece.
Results: The study included 23 patients, 17 female (74%) and 6 male (26%). Age range was 2 to 19 years. Eighteen (18) patients (78.3%) were double heterozygotes for sickle cell and beta thalassemia, 4 (17.4%) were sickle cell homozygotes and 1 patient (4.3%) was double heterozygote for sickle cell disease and hemoglobinopathy D. Out of 23 patients, 4 were on regular blood transfusions due disease related issues (primary prophylaxis for cerebrovascular disease or hypersplenism in 2 cases, severe anemia or repeated pain crises in 2 other cases). No significant difference was recorded in number of hospital visits during the 18month period before and during the pandemic (5.45 visits/year and 6 visits/year, respectively – p = 0.49), reflecting a stable course for patients not receiving regular transfusions and an unaffected by blood shortage or limited hospital access course for regularly transfused patients. To that end, no significant changes were recorded in non-COVID related hospitalizations between the two groups (0.57/year before the pandemic and 0.39/year during the pandemic, p = 0.32). In addition, no difference was found between the reported number of pain crises (0.63 episodes per year vs 0.63 episodes per year, p = 1.0). An otherwise unremarkable overall clinical and laboratory course was reported for all patients during the two time periods compared. No changes in regular monitoring was noted and no changes in drug prescription or drug availability for patients on hydroxyurea was recorded.
Summary-Conclusions: Although sickle cell patients require close monitoring, mostly dependent upon hospital based services, the COVID19 pandemic does not seem to have limited access to recommended care in this patient group.

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P117 THE INTERNATIONAL HAEMOGLOBINOPATHY RESEARCH NETWORK (INHERENT): AN INTERNATIONAL INITIATIVE TO STUDY THE ROLE OF GENETIC MODIFIERS IN HAEMOGLOBINOPATHIES

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Background: Haemoglobinopathies, including sickle cell disease (SCD) and thalassaemia syndromes, represent the commonest monogenic diseases in the world. Although their pathogenicity is well established, the diverse clinical manifestations and the varying degree of severity are less understood and are thought to be governed, in part, by genetic modifiers. Despite the identification and characterisation of a few genetic modifiers by previous studies, these are as yet insufficient to guide treatment recommendations or stratify patients reliably. Larger, multi-ethnic studies are needed to identify and validate further disease modifiers that can be used for patient stratification and personalised treatment. There is a growing need for deeper insight with the availability of novel targeted therapies and potentially curative options like gene therapy in both SCD and thalaessemia.