GMR
The Original

A STUDENT PERSPECTIVE: NEWBORN SCREENING FOR INBORN ERROR OF METABOLISM- CASE STUDY OF METHYLMALONIC ACIDURIA (MMA) USING URINARY GCMS ANALYSIS

Shruti Sharma[1], Uzair Khan[2], Usha Dave[3*]

[1]Student Intern of MILS Labassure International PVT LTD, Mumbai
[2]Graduate Biotech Student, MILS Labassure International PVT LTD, Mumbai
[3*]Research Director, MILS Labassure International PVT LTD, Mumbai

ABSTRACT:
Methylmalonic acidemia (MMA) is a rare autosomal recessive inborn error of metabolism (IEM) caused by defects in Methylmalonyl-CoA mutase activity or cobalamin (Vitamin B12) metabolism, leading to the accumulation of toxic organic acids, mainly increased MMA in blood & urine. Early diagnosis is critical as untreated MMA can result in severe metabolic decompensation, brain damage and death of the baby. This study is aimed to evaluate the incidence, biochemical profile, and diagnostic significance of MMA by metabolic profiling using urinary Gas Chromatography–Mass Spectrometry (GCMS) analysis in a retrospective cohort.
A retrospective observational analysis was conducted on 586 suspected cases referred for metabolic evaluation in Jan-Dec, 2025. Urinary GCMS analysis data, along with clinical records, were assessed to identify metabolic abnormalities. Among the total 586 cases, 34 (5.80%) showed biochemical evidence of MMA, including 5 mass spectrum confirmed cases (0.85%) and 29 possible MMA cases (4.94%) based on the presence of urinary abnormal biomarkers. Elevated urinary Methylmalonic acid, Methylcitrate, and 3-Hydroxybutyrate were key diagnostic markers, with characteristic total ion chromatogram (TIC) patterns supporting disease identification.
The findings highlight MMA as a significant organic acidemia within suspected inborn errors of metabolism and emphasize its variable presentation across different age groups. The study reinforces the importance of expanded newborn screening and confirms urinary GCMS as a reliable gold-standard technique for definitive diagnosis, recommending to include MMA in newborn screening panel. Early detection and timely intervention can thus, be achieved for improving survival and neurodevelopmental outcomes in the affected patients

KEYWORDS: Methylmalonic Aciduria (MMA), IEM, Newborn screening, GCMS, Metabolic profiling

INTRODUCTION

Newborn screening (NBS) is a preventive public health program aimed at identifying congenital metabolic disorders soon after birth, before clinical symptoms appear (1). Inborn Errors of Metabolism (IEMs) are inherited congenital disorders resulting from enzymatic or cofactor deficiencies that disrupt normal metabolic pathways. Although individually rare, collectively they contribute significantly to neonatal and infant disability and death (4). Many developed countries like USA, Australia, Japan, some European, Asian & Arab countries have introduced NBS in their health policies as a mandatory program (1, 4, 5, 16 & 20). The health economists have shown NBS as a cost-effective implementation strategy of national health programs.
The basic NBS disorders screened all over the world are congenital hypothyroidism (CH), congenital adrenal hypoplasia (CAH)., Glucose-6-Phosphate dehydrogenase(G6PD), Biotinidase deficiency, Phenylketonuria (PKU), Cystic Fibrosis (CF) & Galactosemia. The CH, CAH & G6PD are the most common ELISA (Enzyme Linked Immunosorbent Assays) tests which are generally conducted in the basic NBS program (7). The LC-MS/MS technology (TMS) is also used in some countries to increase the coverage of IEM (about 52 IEMs) by testing the air-dried blood spot (DBS) from heel-prick of the newborn (17). Many factors such as frequency of IEM, population size, availability of laboratory infrastructure, metabolic expertise, cost of the test & health priorities of each country decide the selection of NBS disorder list.
India does not have mandatory NBS program in its health policy (7). Indian Council of Medical Research (ICMR) conducted a pilot project to screen one million newborns throughout India for only 2 NBS disorders such as CH & CAH (13). However, few private laboratories and hospitals offer as optional tests after educating parents about the importance of NBS tests (4, 5, 6, 9 & 15).

Inborn Errors of Metabolism (IEM):

IEMs are genetic disorders caused by mutations affecting enzymes, transport proteins, or cofactors involved in metabolism. The concept was first proposed by Sir Archibald Garrod in the early twentieth century. These disorders

may affect carbohydrate, amino acid, fatty acid, or organic acid metabolism (5 & 19) and are generally classified based on the type of the metabolism involved as shown in Table-1.

Table 1: Showing the classification of IEMs

Table 1- Classification of IEMs:
Amino & Organic acid metabolism
Protein metabolism
Carbohydrate metabolism
Lipid metabolism
Pigment metabolism
Mitochondrial disorders
Unknown biochemical defects

(Table 1: Showing the classification of IEMs)

IEMs of Organic Acid Metabolism:

These IEMs are generally referred as organic acidemias or organic acidurias depending on the high level of specific organic acids in blood (acidemia) or in urine (aciduria). There are few common organic acidurias causing disability or death in newborns and children with high frequency (5). The organic acidurias form a major subgroup of IEMs characterized by abnormal accumulation of organic acids and their metabolites in blood and urine (21). These are especially important in neonatal screening because they often present with acute metabolic crisis during infancy but are silent or non-symptomatic in post birth neonatal period (6 & 20). It is therefore very important to add these organic acid disorders in the newborn testing list to detect at the earliest and treat to prevent further health consequences (7 & 23)
The present case report highlights the significance of MMA to be considered as a NBS disorder.

Methylmalonic Aciduria (MMA):

MMA is an inherited metabolic disorder characterized by elevated methylmalonic acid levels in blood and urine due to impaired conversion of methylmalonyl-CoA to succinyl-CoA (11). It is an autosomal recessive organic acidemia caused by defects in Methylmalonyl-CoA mutase activity or abnormalities/ deficiency in cobalamin (Vitamin B12) metabolism. The disease leads to accumulation of Methylmalonic acid and related toxic metabolites. Clinical manifestations include vomiting, lethargy, developmental delay, metabolic acidosis, hypotonia, seizures, and renal complications (11 & 12).
Expanded newborn screening using tandem mass spectrometry (MS/MS) enables early detection of MMA or Propionic acidemia (PA) through elevated propionylcarnitine (C3) levels in dried blood spots. However, differentiation into PA or MMA further requires urinary GCMS analysis which remains a gold standard confirmatory diagnostic method because it provides precise & reliable specific metabolite profiling with their m/z ratios (6, 7 & 14). The rapid screening for organic acidurias based on abnormal patterns of organic acids in neonatal urine by tandem mass spectrometry (TMS) has been reported (23).
Incidence: Globally, the incidence of MMA is reported to be 1.14:100,000 (babyfirsttest.org) (20) & in India the incidence of MMA is reported to be 1:50,000 to 1:100,000 live births (tandfoonline.com) (20). The hospital data of tertiary hospitals give incidence in high-risk/ sick babies (6). There is no genetic epidemiology data in India to reliably offer the incidence.
Biochemical Pathway in MMA metabolism: The MMA has important functional role in organic acid metabolism as shown below in Fig.1-

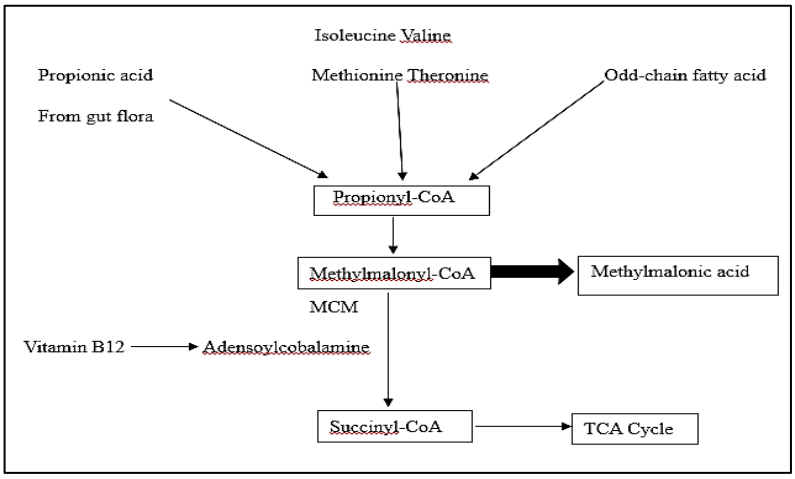

Fig.1- MMA metabolism pathway showing enzyme block (thick black arrow) site.

The conversion of methylmalonyl-CoA to succinyl-CoA requires:

- Methylmalonyl-CoA mutase enzyme
- Adenosylcobalamin (Vitamin B12 derivative)

Defects in these components result in MMA accumulation (11 & 12).

Types of MMA: Depending on the type of defects as shown below, the different types of MMA can occur in patients (Table 2).
Mutase deficiency (mut^0 type OMIM #251000 and mut$^-$ type OMIM #251000)
Cobalamin metabolism defects:

Table: 2- Various types of MMA observed in Patients			
Defect	**Gene**	**OMIM disease**	**OMIM gene**
cblA	MMAA	251100	*607481
cblB	MMAB	251110	*607568
cblC	MMACHC	277400	*609831
cblD	MMADHC	277410	*611935

(Table: 2- Various types of MMA observed in Patients)

The research studies have identified the genes involved with their defects and given specific Mendelian Inheritance number (OMIM) to various MMA subtypes (Table 2).
Clinical Symptoms- The MMA affected newborn is symptomless at birth. The symptoms of severe MMA may appear in neonate but usually appear during infancy and include: poor feeding, vomiting, lethargy, developmental delay, hypotonia, metabolic acidosis, hyperammonemia and renal dysfunction. The babies are immediately admitted to Intensive Care Unit (ICU) for therapy intervention.
Treatment & Management of MMA- Without treatment, MMA may cause irreversible neurological damage or death (3). The treatment includes a protein-restricted diet, carnitine supplementation, and Vitamin B12 therapy in responsive patients. Acute metabolic crises are treated with hydration, glucose and correction of acidosis. Severe cases may require liver transplantation. If detected soon after birth, like in NBS, it improves survival and neurological outcome.

LITERATURE REVIEW:
Methylmalonic aciduria (MMA) is a rare autosomal recessive inborn error of metabolism caused by defects in methylmalonyl-CoA mutase or cobalamin metabolism, leading to the accumulation of toxic metabolites. Early diagnosis is essential, as delayed treatment can result in irreversible neurological damage, developmental delay, metabolic crises, and increased mortality. Expanded newborn screening using tandem mass spectrometry (MS/MS), followed by confirmatory urinary gas chromatography–mass spectrometry (GCMS), is considered the most effective strategy for early detection and diagnosis (3 & 12).
Several studies from India have emphasized the importance of incorporating MMA into newborn screening programmes. Urinary GCMS remains the gold-standard confirmatory test because it accurately identifies disease-specific organic acid biomarkers, including methylmalonic acid and methylcitrate. Early identification and timely treatment with dietary management, carnitine, and vitamin B12 therapy can significantly improve clinical outcomes and reduce long-term neurological complications (7, 8 & 9).

Materials And Methods:
Study Design: This study follows a retrospective, observational research design based on secondary data analysis. The research focuses on analysing existing metabolic data for a period of one year to identify the incidence of MMA in high-risk cases referred to the genetic metabolic laboratory (MILS Labassure International, Mumbai). Also the age onset of symptoms and severity of disease were recorded.

Data Source: The primary dataset consists of anonymised GCMS (Gas Chromatography Mass Spectrometry) test reports provided by the laboratory at which training for GCMS testing was taken by the student (1st Author). These reports include metabolic profiles from:
- Individuals diagnosed with MMA
- Healthy control subjects

All data were de-identified prior to access to ensure patient confidentiality and ethical compliance.

Study Population: The study was conducted in total 586 cases from January to December 2025 who were referred for metabolic evaluation with clinical suspicion of IEM. Out of total 586 cases, the MMA was detected in 34 cases. The age of the patients ranged from 4 different age groups with 19 males and 15 females (Table 3). Clinical data was retrieved from medical records.

METHODOLOGY:
Urine Sample Collection and Process for GCMS analysis: Random urine samples were collected from each patient in sterile containers. Samples were stored at -20 degree C temperatures until analysis. Alternatively, the urine soaked & air- dried filter paper was sent to the laboratory from the remote places/ small towns (Fig. 2) by post. Prior to GCMS analysis, urine samples underwent urease pre-treatment to remove excess urea, followed by chemical

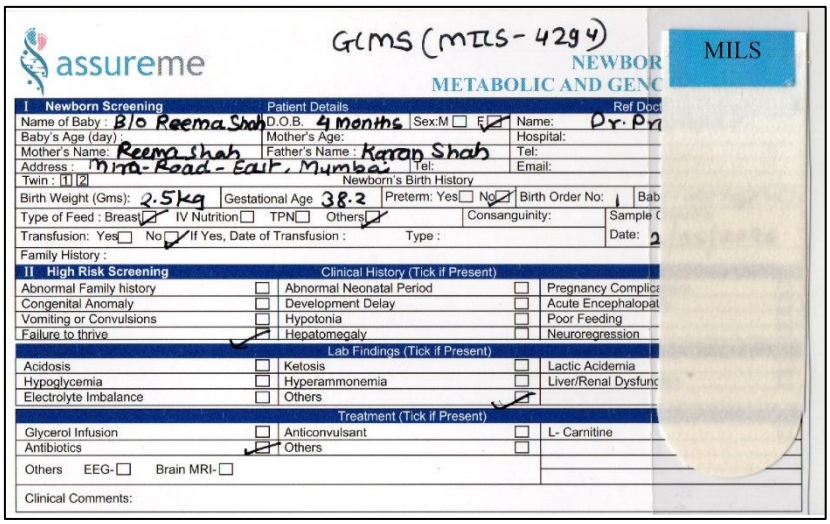

Fig.2: 'Test Request Form' with patient's demographic details &Urine soaked, dried filter paper

derivatization to convert organic acids and other compounds into volatile derivatives suitable for gas chromatographic separation. Standard protocols used in MILS Laboratory for analysis were followed using method of Matsumoto & Kuhara (1996) who had pioneered the current method (14). The test detects almost 250 metabolites comprising different amino acids, organic acids, sugars, sugar alcohols, nucleic acids and fatty acids etc. which serve as biomarkers for various metabolic conditions.

Gas Chromatography–Mass Spectrometry (GCMS) Analysis:

The 2 microL of extract after chemical processing of the urine samples were then injected into GCMS equipment. Separation of metabolites was achieved through gas chromatography and detection was performed using mass spectrometry under electron impact ionization conditions. Total Ion Chromatograms (TICs) were generated for each sample, enabling comprehensive profiling of urinary metabolic compounds.

Identification of metabolites was performed by comparing retention times and m/z mass spectral patterns using established reference libraries. Particular attention was given to the identification and quantification of Methylmalonic acid (MMA), 3-Hydroxybutyrate (3HB), Methylcitrate (Me-Citrate) & 2, 3-Dihydroxy-2-Methylbutyrate which are the key biochemical markers of MMA. Quantitative analysis of MMA and its metabolites was performed, and values were compared against already established laboratory reference ranges. Markedly elevated urinary MMA levels were considered diagnostic of Methylmalonic Acidemia.

RESULTS:

GC-MS findings were correlated with clinical presentation and laboratory results. Elevated urinary MMA levels were interpreted as diagnostic of MMA in the appropriate clinical context with mass spectrum (Fig. 3). Out of total 586 referral cases, 34 were found to be MMA (5.8%), as the first most common organic acidemia (Table 3). On further analysis, about 1% (5 out of 586) appeared to be with severe Methylmalonyl-CoA mutase enzyme deficiency as mass-spectrum confirmed it & 4.94 % (29 out of 586) appeared to be with high possibility of MMA with co-factor deficiencies (Table 3).

Among the positive 34 MMA cases, the severely affected MMA were 15 % (5 out of 34), and the remaining 85 % MMA cases were due to cofactor deficiencies (29 out of 34). These cases were responsive to Vit.B12 and carnitine therapy with improvements in symptoms.

Table 3 summarizes the results of clinical & GCMS urinary screening of total 34 MMA cases which were divided into 4 age groups (Table 3).

Table 3: Total Referral GCMS CasesN = 586 (Period- Jan-Dec.2025)

N=34 MMA Cases Diagnosed - 5.8 % (out of 586)
Male=19; Female=15

MMA Confirmed diagnosis Cases N= 5/34 (15%)		**MMA with Cofactor deficiencies N=29/34 (85%)**		
Sr. No	**Age Group**	**Severe MMA Cases N = 5/34 (15%)**	**MMA Cases due to Cofactor def. N = 29/34 (85 %)**	**Total MMA Cases N = 34/586 (5.80%)**
1.	Below 1 Month	1	6	7
2.	1 Month- 6 Months	1	6	7

3.	6 Months- 5 Years	0	9	9
4.	5 Years-12 Years & above	3	8	11
	Total	**5**	**29**	**34**

(Table 3 summarizes the results of clinical & GCMS urinary screening)

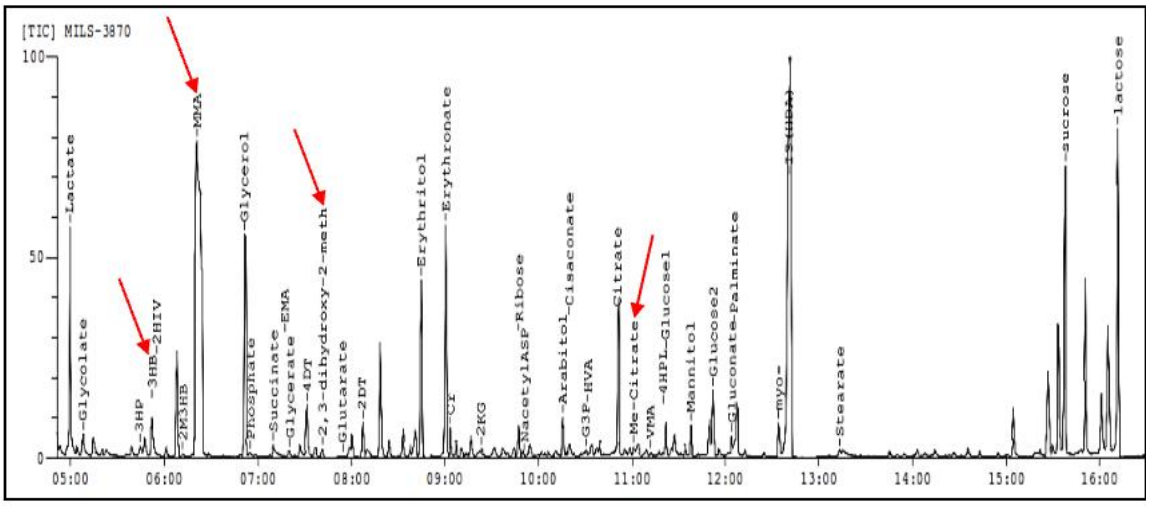

Fig. 3- This is a TIC of the severe MMA case showing increased abnormal metabolites

The TIC of the MMA confirmed case showed the high peaks of 3-Hydroxybutyrate (3HB), Methylmalonic acid (MMA), 2, 3-Dihydroxy-2-Methylbutyrate & Methylcitrate (Me-Citrate) (4 red arrows) i.e. a key biochemical markers of Methylmalonic Acidemia (Fig.3).

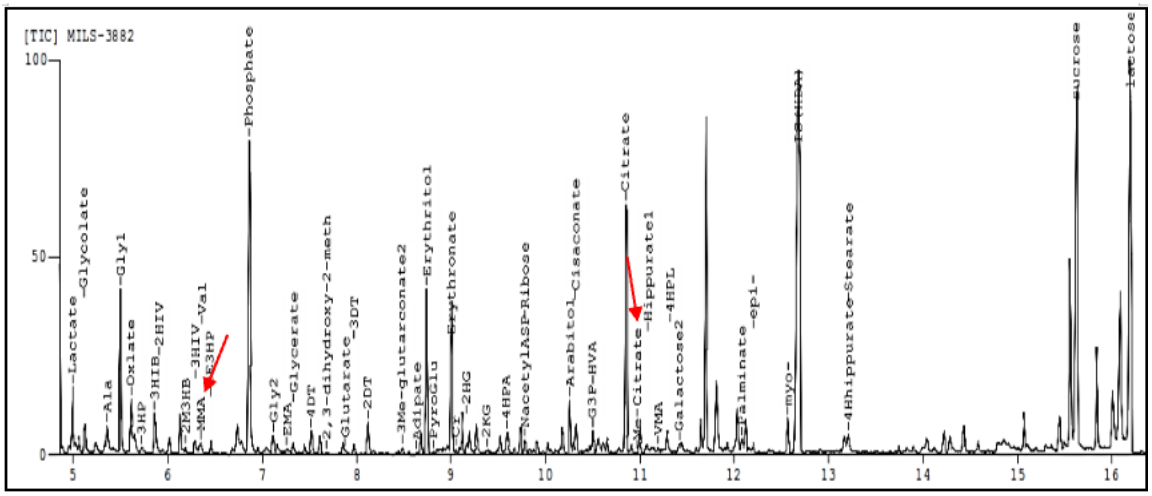

Fig: 4-This is a TIC of MMA case due to Co-factor deficiency

The TIC of the patient (Fig: 4) shows MMA with strong possibility. The mildly increased peaks of Methylmalonic acid (MMA) & Methylcitrate (Me-Citrate) are visible (2 red arrows) and these two biochemial markers indicate presence of Methylmalonic Acidemia with Vit.B12 cofactor deficiencies (Table 4).

Table 4 – Comparative Quantitative values of MMA biomarkers

Biomarkers	Control	MMA Cofactors Def.	Severe MMA
3-Hydroxybutyrate (3HB)	Absent	Absent	3.760
Methylmalonic Acid (MMA)	Absent	1.311	19.601
2,3-Dihydroxy-2-Methylbutyrate	Absent	Absent	0.2290
Metylcitrate (Me-Citrate)	Absent	1.690	2.043

(Table 4 – Comparative Quantitative values of MMA biomarkers)

DISCUSSION:

The severe cases of MMA due to defects in Methylmalonyl-CoA metabolism, leading to accumulation of toxic metabolites and neurological damage were 5 (15%) in the present study. These patients showed lethargy, metabolic acidosis, vomiting, and developmental delay. There is enough evidence that metabolite accumulation affects brain

development and may cause seizures and cognitive impairment (10). It is a noteworthy finding that 21 out of 29 cases (72%) were below 5 years of age indicating early onset of MMA due to cofactor deficiencies.
Similarly, 2 out of 5 (40 %) severe MMA cases were detected in the neonate period (below 6 months of age) which makes early detection & therapy management possible with minimal damage due to toxic accumulation of products. Protecting the brain from toxic metabolites is very important and critical in early days of life for proper brain growth.
The 29 of 34 MMA cases (85 %) were responded to Vit. B12 & thereby could be saved from further deterioration & disabilities, mainly due to early, accurate & reliable GCMS diagnosis (7). In the absence of special diet formula, the high doses of Vit.B12, carnitine and protein restriction diets and clinical as well as laboratory monitoring for abnormal metabolites were helpful in saving life of MMA affected babies.
The high incidence (5.8%) of MMA is corroborated by other studies, making it among the most common organic acidurias found in the Indian population (7 & 9). Consanguinity increases the risk of inheritance of the disease. Furthermore, demographically stable and isolated communities have an increased risk of inbreeding, so prevalent in many parts of India. This higher incidence rate suggests that MMA should be considered for inclusion in Newborn Screening Programmes in India, as also emphasised by other Indian study of 25 years of GCMS urinary metabolic screening experience in India (7).
Furthermore, the results also emphasized the frequency of the two possible causes of the MMA disorder. Out of the 34 positive cases, 29 were linked to cofactor deficiencies, indicating a definite possibility of MMA which is consistent with the published report (2), linking cobalamin cofactor deficiency to biochemically confirmed elevations in methylmalonic acid in over half of infants. This study conducted in Bhaktapur, Nepal found elevated MMA with low cobalamin status, supporting the interpretation that cofactor insufficiency in our cohort may be linked to MMA risk due to nutritional factor (2).
The 5 out of 34 cases were confirmed as definite methylmalonic aciduria due to severe methylmalonyl-CoA mutase deficiency, consistent with the Vitamin B12-unresponsive mut0/mut– subtype, though DNA mutation test was not feasible in these MMA cases. However, a study conducted in China found a positive correlation between Vitamin B12 unresponsiveness and poorer long-term outcomes and mortality, underscoring the clinical importance of early molecular confirmation of the disease (11).
Noteworthy finding was that the majority of the MMA cases were identified before the age of 5 years. Thus, newborn screening is imperative for physicians to provide treatment that prevents lethal neurological damage. Early detection and diagnosis followed by proper therapy can substantially reduce disease severity (3).
GC-MS, as a method of biochemical screening, has been successfully utilized to analyze multiple metabolic intermediates in urine, providing diagnostic evidence for over 130 inborn errors of metabolism, making it a suitable tool for detecting MMA and PA (5 ,7 & 9). Indeed, the 2021 European consensus guidelines for MMA and PA identify urine organic acid measurement as a high-quality, strongly recommended step for achieving a reliable diagnosis of these disorders (12 & 23). Despite this, its application remains limited to specialized medical centres due to the requirement for advanced instrumentation and expertise.
In an ideal scenario, genetic testing (DNA mutation) would be administered for all the positive MMA cases to confirm the precise molecular diagnosis. For now, however, since no cure currently exists for MMA, early diagnosis by urinary GCMS screening and cofactor treatment remain the most effective means of preventing irreversible brain damage in Indian subjects. Treatment of MMA includes dietary protein restriction, carnitine supplementation, Vitamin B12 therapy, and management of metabolic crises. Early diagnosis and treatment significantly improve survival and quality of life in the affected patients (10).
Newborn screening helps in early identification of MMA before severe complications develop. Tandem MS/MS (TMS) is used for initial screening, while urinary GCMS confirms diagnosis by detecting elevated Methylmalonic acid and related metabolites. Children diagnosed early through newborn screening show better neurodevelopmental outcomes and fewer brain abnormalities (3, 18). Newborn screening is the need of hour in India has been emphasized (4, 5, & 22) and also the need in developing countries is demonstrated (7, 8 & 20). The cohort study by the present referral laboratory in India offered the evidence of 12 preventable common IEMs with high incidence (1 in 26 to 200- 400), recommending the comprehensive panel using mass spectrometry for NBS program in India. The MMA is shown to be the most common organic aciduria in 25 years of their study with incidence of 1: 26 in sick babies referred to the laboratory where the student authors of this paper worked (7).

CONCLUSION:
Methylmalonic Acidemia is a severe but potentially manageable Inborn Error of Metabolism if diagnosed early. Urinary GCMS analysis remains a gold standard confirmatory method for MMA due to its ability to identify characteristics organic acid profiles. Studies on neurodevelopmental outcome demonstrate that early diagnosis through newborn screening significantly improves prognosis and reduces brain injury. From a student perspective, MMA provides an excellent model of understanding biochemical genetics, metabolic disorders, analytical techniques, and the importance of prevention of childhood disability or death. Since the newborn screening program plays a crucial role in early detection and prevention of childhood disability/death, the present case report highly recommends MMA to include in the NBS list considering current Indian health scenario.

ACKNOWLEDGEMENT: We are grateful to the staff of MILS Labassure International, Mumbai for their cooperation & support during this study.

REFERENCES

1. American Academy of Paediatrics (AAP): Newborn Screening Task Force: Serving the family from birth to the medical home-newborn screening: a blueprint for the future. Paediatrics 2000, 106: S383-S427.
2. Chandyo RK, Ulak M, Kvestad I, Hysing M, Shrestha M, Ranjitkar S, Ulvik A, Ueland PM, Shrestha L, Strand TA. Cobalamin and Folate Status among Breastfed Infants in Bhaktapur, Nepal. Nutrients. 2018 May 18;10(5):639. doi: 10.3390/nu10050639.
3. Chen T, Gao Y, Zhang S, Wang Y, et al. Methylmalonic acidemia: Neurodevelopment and neuroimaging. Front Neurosci. 2023 Jan 26; 17:1110942.
4. Dave UP, Das B.R.: Newborn screening- From 'Guthrie age to Genomic age'. J. Obst. & Gynaecology of India. 2010, 60-3: 210–220.
5. Dave U P: Genetic Counseling Approach in Inborn Errors of Metabolism, in Dave UP & Shetty DL (eds): Genetic counseling- clinical & laboratory approach., Jaypee Brothers Medical Publishers, 2022, p.219.
6. Dave UP: Screening and Diagnosis of Inborn Errors of Metabolism, in Sahetya R, Malhotra J and Purandarey H (eds): Principles and practice of fetal medicine, Jaypee Brothers Medical Publishers, 2016, p.105.
7. Dave UP & Zhang C: A Comprehensive NBS Approach for 12 Common IEMs in India: Recommendation based on 25 Years of Diagnostic Experience in Mass Spectrometry. J Medical Mass Spectrometry -Newborn Screening and Mass Spectrometry 2025, Vol. 9 No. 2, 1-14.
8. Gaikwad S, Ganvir S, Uke P: Newborn Screening in Developing Countries: The Need of the Hour. Cureus May 03, 2024, 16(5): e59572. DOI 10.7759/cureus.59572.
9. Hampe MH, Panaskar SN, Yadav AA, Ingale PW. Gas chromatography/mass spectrometry-based urine metabolome study in children for inborn errors of metabolism: An Indian experience. Clinical biochemistry. 2017, 50(3):121-126.
10. Head PE, Meier JL, Venditti CP.: New insights into the pathophysiology of methylmalonic acidemia. Journal of Inherited Metabolic Disease. 2023; 46(3):436–449.
11. Ling S, Wu S, Shuai R, Yu Y, Qiu W, Wei H, Yang C, Xu P, Zou H, Feng J, Niu T, Hu H, Zhang H, Liang L, Wang Y, Chen T, Xu F, Gu X, Han L. Clinical outcomes of patients with mut-type methylmalonic acidemia identified through expanded newborn screening in China. Hum Genomics. 2024 Jul 29;18(1):84. doi: 10.1186/s40246-024-00646-0.
12. Manoli I, Sloan JL, Venditti CP. Isolated Methylmalonic Acidemia. 2005 Aug 16 [Updated 2022 Sep 8]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. Gene Reviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026.
13. Mathur R. New born screening program in India: ICMR multicentric experience. Mol Cytogenet. 2014 Jan 21;7: I40. doi: 10.1186/1755-8166-7-S1-I40.
14. Matsumoto I. and Kuhara T.: A new chemical diagnostic method for inborn errors of metabolism by Mass Spectrometry- Rapid, Practical, and simultaneous urinary metabolites Analysis. Mass Spectrometry Reviews, 1996. 15, 43-57.
15. Mookken T: Universal implementation of newborn screening in India. International journal of neonatal screening 2020, 25, 6(2):24 DOI: 10.3390/ijns6020024.
16. Padilla CD, Therrell BL.: Newborn screening in the Asia Pacific region. J Inherit Metab Dis. 2007, 30: 490-506.
17. Rashed MS, Ozand, PT, Bucknail MP, & Little DT: Diagnosis of inborn errors of metabolism from blood spots by acylcarnitines and amino acids profiling using automated electrospray tandem mass spectrometry. Pediatr. Res 1995, 38 (3): 324- 331.
18. Ricci D, Martinelli D, Ferrantini G, Lucibello S, et al. Early neurodevelopmental characterization in children with cobalamin C/defect. J Inherit Metab Dis. 2020 Mar; 43(2):367-374.
19. Sabitha Vadakedath, Venkataramana Kandi, Vikram Godishala, Venkata Bharat Kumar Pinnelli, Samar Sami Alkafaas, and Sara Sami EIkafas, "The Principle, Types, and Applications of Mass Spectrometry: A Comprehensive Review." Biomedicine and Biotechnology, vol. 7, no. 1 (2022): 6-22. doi: 10.12691/bb-7-1-2.
20. Shibata N, Hasegawa Y, Yamada K, Kobayashi H, Purevsuren J, Yang Y, Dung VC, Khanh NN, Verma IC, Bijarnia-Mahay S, Lee DH, Niu DM, Hoffmann GF, Shigematsu Y, Fukao T, Fukuda S, Taketani T, Yamaguchi S. Diversity in the incidence and spectrum of organic acidemias, fatty acid oxidation disorders, and amino acid disorders in Asian countries: Selective screening vs. expanded newborn screening. Mol Genet Metab Rep. 2018 May 21; 16:5-10. doi: 10.1016/j.ymgmr.2018.05.003.
21. Vaidyanathan K, Narayanan MP, Vasudevan DM. Organic Acidurias: An Updated Review. Indian Journal of Clinical Biochemistry. 2011; 26(4):319–325.
22. Verma IC, Bijarnia-Mahay S, Jhingan G, Verma J: Newborn screening: need of the hour in India. Indian J Pediatrics 2015, 82: 61–70.
23. Zhongping Huang, Zhenzhen Hu, Chaochao Tu, et al.: Rapid screening for organic acidurias based on abnormal patterns of organic acids in neonatal urine by tandem mass spectrometry with automated flow injection. Microchemical Journal, 2021, Vol. 171, 106871.