

A systematic review and meta-analysis on urinary biomarkers in myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) generally focuses on whether urine tests show consistent biochemical patterns that could help distinguish ME from healthy controls or other conditions.

Across studies included in this type of review, the most commonly reported signals tend to fall into a few recurring areas:

1. Metabolic dysfunction (metabolomics changes)

- *Alterations in energy metabolism markers, including metabolites linked to glycolysis and the Krebs cycle

- *Changes in amino acids (suggesting altered protein turnover or stress metabolism)

- *Differences in acylcarnitines, which are involved in mitochondrial fatty acid transport and energy production

These findings are often interpreted as consistent with impaired cellular energy metabolism, though results vary between studies.

2. Oxidative stress and redox imbalance

- *Elevated or altered urinary markers related to oxidative stress (such as products of lipid peroxidation in some studies)

- *Shifts in compounds linked to antioxidant pathways, suggesting increased oxidative burden or altered detoxification responses

3. Purine and nucleotide metabolism

- *Some studies report changes in metabolites related to ATP breakdown and purine metabolism, which is relevant given hypotheses around impaired energy availability and exertional intolerance in ME/CFS

4. Microbial and gut-related metabolites (less consistent)

- *A smaller subset of studies identifies differences in microbiome-derived metabolites, though findings are inconsistent and depend heavily on methodology

What the meta-analysis usually concludes

- *There is no single, validated urinary biomarker for ME/CFS yet

- *However, there is moderate evidence of reproducible metabolic dysregulation patterns, especially involving energy metabolism and oxidative stress

- *The biggest limitation is heterogeneity: different diagnostic criteria (Fukuda vs ICC/CCC), small sample sizes, and varied lab methods make results hard to combine cleanly

Key takeaway

Urine studies don't point to one diagnostic marker, but they do repeatedly suggest that ME/CFS is associated with systemic metabolic disruption rather than isolated "fatigue" biology, particularly involving energy production pathways.

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1) Specific urinary biomarkers reported in ME/CFS studies

Across metabolomics and smaller targeted studies, the same categories of compounds show up repeatedly rather than one single marker.

Energy metabolism / mitochondrial-related compounds

These are among the most discussed:

- *Lactate (and lactate-related metabolites)

which suggests increased reliance on anaerobic metabolism in some patients

- *Pyruvate (and lactate/pyruvate ratio changes) which reflects altered glycolysis–mitochondrial balance

- *Acylcarnitines (various chain lengths)

are involved in fatty acid transport into mitochondria. Some studies show reduced or dysregulated excretion patterns

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Amino acids and protein metabolism

*Altered urinary levels of:

- *Glutamine / glutamate

- *Phenylalanine / tyrosine

- *Branched-chain amino acids (valine, leucine, isoleucine derivatives)

*Often interpreted as:

- *increased protein breakdown

- *altered nitrogen handling

- *stress-response metabolism changes

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Purine / ATP breakdown markers

These are frequently highlighted in ME/CFS metabolomics:

- *Uric acid pathway metabolites
- *Hypoxanthine and xanthine derivatives
- *Other purine degradation products

These support the idea of altered energy currency (ATP) turnover, especially under physiological stress.

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Oxidative stress–related metabolites

- *Lipid peroxidation products (varies by study design)
- *Changes in compounds linked to glutathione metabolism
- *Indicators of redox imbalance and detoxification load

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Microbiome-related metabolites (in some studies only)

- *Short-chain fatty acid derivatives (inconsistent findings)
- *Phenolic compounds from gut bacteria metabolism

These are not yet reproducible enough for clinical use.

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2) How urinary findings compare with blood and muscle studies. A useful way to think about this is: urine reflects what the body is discarding, while blood and muscle reflect what is happening inside tissues.

A. Blood (plasma/serum metabolomics)

Blood studies tend to show more direct and consistent patterns than urine:

Common findings:

- *Reduced amino acid availability
- *Lower levels of TCA cycle intermediates
- *Altered lipid metabolism (phospholipids, acylcarnitines)
- *Evidence of a shift toward a hypometabolic state in some cohorts

Relationship to urine:

- *Urine often shows the downstream “waste signature” of these same disruptions

*Blood changes are usually more stable and easier to reproduce than urinary ones

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B. Muscle tissue studies (biopsy and exercise physiology work). Muscle studies are especially relevant because exertion intolerance is central in ME.

Findings include:

*Reduced oxidative phosphorylation capacity

*Evidence of mitochondrial dysfunction or reduced efficiency

*Abnormal lactate accumulation during low-level exertion

*Possible impaired oxygen utilization or microcirculatory delivery

*Post-exertional abnormalities in gene expression and metabolism

Relationship to urine:

*Urinary lactate and purine metabolites can reflect muscle energy stress indirectly

*But muscle findings show the source problem, while urine shows systemic spillover effects

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Putting it together (integrated view)

Across all three biological layers:

*Muscle = where the energy failure is most functionally evident

*Blood = circulating metabolic disruption profile

*Urine = excreted footprint of that systemic metabolic stress

A consistent theme across studies is not a single abnormal pathway, but a pattern of:

‘Reduced metabolic flexibility + impaired energy production under demand.

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Important limitation across all studies

*Most cohorts are small

*Diagnostic definitions vary (Fukuda vs ICC vs CCC)

*Physical activity levels before sampling are rarely controlled tightly

*This contributes to inconsistent replication, especially in urine studies

For more information, see

<https://m.facebook.com/groups/1063785371126868/permalink/2177933133045414/?>

Pattern testing ;

<https://m.facebook.com/groups/1063785371126868/permalink/2177937893044938/?>

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