

# Elevated serum sialic acid in pregnancy

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## Abstract

**Objective**—Serum sialic acid has recently gained interest as a possible cardiovascular risk factor as well as a potential tumour marker. The effect of pregnancy on serum sialic acid is unclear particularly in the post-partum period.

**Design**—Longitudinal cohort.

**Setting**—Teaching hospital antenatal clinic.

**Population**—29 pregnant women, 27 age matched non-pregnant women.

**Methods**—Specific enzymatic assay for sialic acid. The first serum sample was taken between 37 and 42 weeks of gestation; in 22 women this was followed by a second serum sample at 12 weeks post-partum. Serum sialic acid concentration was also measured in the 27 controls.

**Results**—Mean (SD) serum sialic acid concentration was higher during pregnancy than post-partum: 91.1 (11.1) v 77.5 (11.1) mg/dl ( $p < 0.001$ ); or in the control group: 66.0 (9.7) mg/dl ( $p < 0.001$ ).

**Conclusions**—Serum sialic acid is elevated during pregnancy and post-partum.

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Keywords: pregnancy; sialic acid; cardiovascular risk factor

Sialic acid is the generic term given to a family of acetylated derivatives of neuraminic acid. Sialic acids have a number of major biological functions<sup>1</sup>: their large electronegative charge has implications for the electronegativity of cells; they are found as essential components of many cell surface receptors; they have some influence on glycoprotein conformational states; they are often part of antigenic determinants of glycolipids or glycoproteins; they prevent ligands from recognising receptors.

Serum sialic acid has been used as a tumour marker for a number of different types of cancer: carcinoma of the bronchus, prostate, ovary, breast, colon, and malignant melanoma.<sup>2-5</sup> In addition, serum sialic acid has been found to be elevated in chronic liver diseases, pneumonia, rheumatoid arthritis, Behcet's disease, and Crohn's disease.<sup>6-9</sup> Patients with chronic glomerulonephritis<sup>10</sup> also have elevated serum sialic acid concentrations. Serum sialic acid has been recently shown to be a cardiovascular risk factor and elevated in patients with an acute myocardial infarction although the underlying mechanism is not known.<sup>11 12</sup>

This study tested the hypothesis that serum sialic acid may be altered in pregnancy. There are few data concerning serum sialic acid in

pregnancy or post-partum and controversy exists regarding whether there is an elevation during and following pregnancy. Such a study has important implications for the interpretation of serum sialic acid status in females.

## Methods

### SUBJECTS

Twenty nine pregnant women were studied, mean (SD) age 30.3 (4.6) years. The first serum sample was taken between 37 and 42 weeks of gestation; in 22 women this was followed by a second serum sample at 12 weeks post-partum. Twenty seven age matched (28.3 (5.4) years) non-pregnant women formed a control group. All subjects were healthy at the time of study with no history of malignant or inflammatory disease, or myocardial infarction. None of the females was on hormonal therapy during the study. We had ethical committee approval for the taking of blood in these subjects.

### ASSAYS

Serum sialic acid was assayed by an enzymatic method purchased from Boehringer Mannheim (Lewes, Sussex, UK) adapted for use on a Roche Cobas Bio or Fara analyser (Roche, Welwyn, Herts, UK). This method uses a coupled enzyme assay reaction, incorporating neuraminidase, N-acetylneuraminic acid aldolase, and pyruvate oxidase linked to a peroxidase dye system. The between batch coefficient of variation (CV%) was about 3.5% or better.

### STATISTICAL ANALYSIS

To compare group means the Student's *t* test was used. Statistical significance was taken as  $p < 0.05$ . Results are shown as mean (SD).

## Results

Serum sialic acid was higher in the pregnant subjects ( $n = 29$ ) than the non-pregnant control ( $n = 27$ ) group: 91.1 (11.1) v 66.0 (9.7) mg/dl ( $p < 0.001$ ). Serum sialic acid values were also higher in the post-partum group ( $n = 22$ ) than in the control group: 77.5 (9.9) v 66.0 (9.7) mg/dl ( $p < 0.001$ ). Serum sialic acid values during pregnancy were higher than those in the same cohort of women post-partum: 91.1 (11.1) v 77.5 (9.9) mg/dl ( $p < 0.001$ ).

## Discussion

The serum sialic acid concentrations obtained by us in this study are similar to those reported by Hangloo *et al*<sup>13</sup> and Lindberg *et al*<sup>14</sup> who reported serum sialic acid values in non-

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pregnant females. However, we used a different assay that is probably more specific for sialic acid as it is based on an enzymatic method.

We were able to show that there were highly significant elevations in serum sialic acid during pregnancy which persisted 12 weeks post-partum, albeit to a lesser degree in comparison to non-pregnant females. There is controversy in the literature of whether serum sialic acid increases in pregnancy. Sydow *et al*<sup>15</sup> reported that serum sialic acid was not significantly increased in pregnancy, whereas Alvi and colleagues<sup>16</sup> did show significant elevation during pregnancy that was in keeping with earlier data from Goni and co-workers.<sup>17</sup> There could be many reasons for these discrepancies including varying populations of women studied and assay differences. We used a specific enzymatic assay to measure serum sialic acid and not the thiobarbituric acid or resorcinol assays that are colorimetric and can interfere with other carbohydrate moieties.

The mechanism of alterations in sialic acid concentrations is unclear and merits further research as to its cause. A number of alterations in sialic acid metabolism have been described during pregnancy. Szeverenyi *et al*<sup>18</sup> showed that the binding of sialic acid targeting lectins (*Limulus polyphemus* and *Triticum vulgare*) towards uterine cervical tissue is increased during pregnancy. Nemansky *et al*<sup>19</sup> demonstrated that human placenta has sialyltransferase activity that is capable of transferring sialic acid residues to oligosaccharide chains of glycoproteins. Furthermore, Arkwright *et al*<sup>20</sup> described fetally derived syntiotrophoblast tissue in the placenta as being richly sialylated.

Interestingly, bovine pregnancy associated glycoprotein also contains sialic acid residues, although whether the same applies to humans needs clarification.<sup>21</sup> Furthermore, salivary sialic acid is decreased during pregnancy, which the authors concluded may be because of the hormonal changes associated with pregnancy.<sup>22</sup>

The elevation of serum sialic acid during pregnancy is of note and we believe our data adds to the literature showing changes in sialic acid status in pregnancy. The mechanisms are unclear and we can only speculate as to the reason. Particularly, intriguing is the question of whether pregnancy imposes an increased risk of cardiovascular disease<sup>23, 24</sup>; in this context serum sialic acid has been reputed to be a strong cardiovascular risk factor.<sup>11, 14</sup> However, prospective studies are required to test this hypothesis and the place, if any, of measuring serum sialic acid in pregnant women.

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