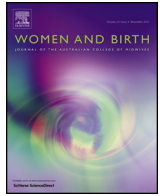




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### ORIGINAL RESEARCH – QUANTITATIVE

# Does eating oily fish improve gestational and neonatal outcomes? Findings from a Sicilian study

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#### ABSTRACT

**Background:** Fish is a source of long-chain polyunsaturated n-3 fatty acids, but it may also contain a number of pollutants.

**Methods:** Between April and July 2013, we selected 114 women who gave birth to living babies, and divided them according to type and frequency of the fish consumed. We evaluated both gestational and neonatal outcomes. Docosahexaenoic acid (DHA) supplementation was taken into account.

**Findings:** One hundred and four women (91.2%) consumed fish on the average of 4.7 times/month, while 10 (8.8%) did not consume fish at all. Fifty-nine women (51.8%) were taking supplements containing DHA (200 mg/day), almost all of whom ( $n = 55$ ) consumed fish. Pregnancy induced hypertension was more frequent in non-fish eaters than in fish eaters (20% vs 4.8%,  $P = 0.056$ ).

Consumption of small size oily fish correlated positively with both neonatal weight ( $r = 0.195$ ,  $P = 0.037$ ) and head circumference ( $r = 0.211$ ,  $P = 0.024$ ). In contrast, consumption of lean fish or shellfish correlated negatively with neonatal head circumference ( $r = 0.206$ ,  $P = 0.028$ , or  $r = 0.192$ ,  $P = 0.041$ ).

**Discussion:** These data agree with previous observational studies and reinforce the protective role of small oily fish consumption on preterm birth risk, neonatal weight, length and head circumference.

**Conclusion:** Small oily fish consumption should be favored over other types of fish.

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## 1. Introduction

Fish is a source of long-chain polyunsaturated n-3 fatty acids and its consumption is associated with prolonged length of gestation, decreased pre-term birth rates, increased birth weight.<sup>1–16</sup> However, fish may contain a number of pollutants.<sup>2–6</sup> This is the first study in our geographical area on fish consumption in pregnant women and its influence on gestational and neonatal outcomes, taking into account the different categories of seafood and DHA

supplementation. In agreement with previous observational studies, we show that fish consumption correlates inversely with prevalence of pregnancy induced hypertension (PIH). We also show that small fish oil consumption is associated with increased neonatal weight and neonatal head circumference (NHC), while lean/shellfish consumption is associated with decreased NHC.

Fish is a major source of nutrients such as proteins, long-chain polyunsaturated n-3 fatty acids (LCPUFA), selenium, iodine, and vitamin D, which are considered to be beneficial for fetal growth and development.<sup>1</sup> However, fish is also a well-known route of exposure to pollutants such as dioxins, polychlorinated biphenyls, methylmercury and other heavy metals, which may adversely affect gestational length, fetal growth and birth outcomes.<sup>2–6</sup> Because fish contains both favorable and unfavorable substances, the net effect of its consumption during pregnancy is still uncertain.

**Abbreviations:** DHA, docosahexaenoic acid; FDA, Food and Drug Administration; GDM, gestational diabetes mellitus; LCPUFA, long-chain polyunsaturated n-3 fatty acids; NHC, neonatal head circumference; PE, preeclampsia; PIH, pregnancy induced hypertension; SGA, small for gestational age.

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Observational studies and clinical trials have shown that seafood consumption, or supplementation with LCPUFA or fish oil are associated with prolonged length of gestation, decreased pre-term birth rates,<sup>7–13</sup> increased birth weight,<sup>8,9,12–16</sup> and reduced rates of newborns small for gestational age (SGA).<sup>16</sup> However, studies on the associations between maternal fish consumption and birth outcomes are contrasting.<sup>7,16–19</sup> Contrasting are also data on the risk of developing diabetes mellitus or impaired glucose tolerance in relation to the supplementation with LCPUFA in pregnancy and beyond pregnancy.<sup>20–24</sup> This discrepancy has been partly attributed to the different content in certain substances among different types of fish. For instance, fatty fish contains larger amounts of the beneficial LCPUFA and similar to shellfish, larger amounts of pollutants.<sup>4,25–27</sup>

In some clinical studies, docosahexaenoic acid (DHA) was supplied to pregnant women with mixed results observed concerning gestational and neonatal outcomes.<sup>28,29</sup> This variability could be explained by the different doses of DHA administered and the different intake of DHA by food.

The hypothesis that fish oil might be protective against pregnancy induced hypertension (PIH) dates back to the 1990s, when LCPUFA were reported to increase vasodilation and decrease platelet aggregation,<sup>30</sup> though subsequent data were conflicting.<sup>31–35</sup> Furthermore there is still uncertainty regarding the efficacy of increased intake of n-3 LCPUFA during pregnancy in reducing the risk of gestational diabetes mellitus (GDM) and preeclampsia (pregnancy induced hypertension and proteinuria) (PE).<sup>36</sup>

Recently, a number of studies have balanced the potential risks and benefits of fish consumption: fish and seafood intake is the dominant human exposure to MeHg, that can have serious adverse effects on the nervous and cardiovascular systems; maternal intake of fish has modest beneficial effects on neurodevelopmental and cognitive outcomes of offspring.<sup>37</sup>

In contrast to the vast international literature on the effects of exposure to metal mercury from fish consumption during pregnancy,<sup>2–4,38–41</sup> few Italian studies are available.<sup>42,43</sup>

Considering the lack of studies in our geographical area, we aimed at evaluating fish and DHA supplements consumption in a North-Eastern Sicilian pregnant cohort. We also aimed at assessing the influence of fish consumption and DHA supplementation on gestational duration, preterm birth, PIH, GDM, neonatal weight, length and head circumference.

## 2. Methods

Between April and July 2013, upon informed consent, 317 pregnant women were contacted at 34th week of gestation, at the Division of Obstetrics and Gynecology of our University Hospital. For the purpose of selecting the study group, we administered a detailed questionnaire about the socioeconomic status, lifestyle, family history, personal and midwife history. For the purpose of outcomes, we evaluated intake of multivitamin and/or DHA supplements and fish consumption (see below).

Out of 317 women, we selected 114 women who gave birth to a singleton live baby. Inclusion criteria were: (1) to be a Caucasian non-immigrant woman born and living in our province; (2) to have stable dietary habits and normal weight; (3) to consume fish unfried at home, if they were fish eaters. Exclusion criteria were: (1) to be of disadvantaged socioeconomic status; (2) to be smoker and to have a history of drug/alcohol abuse; (3) family and personal history of diabetes; (4) personal history of recurrent miscarriage, diabetes or preeclampsia in previous pregnancies, thrombophilia, anemia, chronic hypertension, infections of the lower urinary tract.

Dietary assessment was carried out at the first visit, by a face-to-face interview using an Italian food frequency questionnaire<sup>44</sup> with the assistance of color photographs to show portion size.<sup>45</sup> We also assessed the adherence to the Mediterranean diet.<sup>46</sup> Monthly frequency of maternal fish intake was categorized as follows: never or less than once, 2–4 times, 5–8 times and  $\geq 9$  times.

We considered four types of fish: (A) large size oily fish with both high DHA and mercury content (tuna, swordfish), (B) small size oily fish with high DHA, low mercury content (mackerel, salmon, anchovy, garfish, spatula, sardine), (C) lean fish with low DHA and medium mercury content (sea gill-head bream, sea bass, cod, sea bream, perch), and (D) shellfish with low DHA, and low mercury content.<sup>47–49</sup>

We evaluated gestational and neonatal outcomes. Gestational outcomes were gestational duration; complications during pregnancy: preterm birth, PIH, GDM; complications at delivery and mode of delivery. Neonatal outcomes were: neonatal weight, height and head circumference (NHC).

### 2.1. Informed consent

This study was based on a practice improvement project. All volunteers signed a consent form to declare a voluntary agreement with all procedures implicated in this project. Participants were informed that their participation could be voluntarily terminated at any time without any consequence to the woman or to the quality of her health care. All information obtained from research volunteers were treated as confidential. Only 6 of the 317 women declined to participate.

### 2.2. Statistical analysis

Data are reported as mean  $\pm$  SD, median and range. Differences between means of two or more groups were compared with the Mann–Whitney test or the Kruskal–Wallis test. We used the non-parametric Spearman correlation coefficient to assess statistical dependence between numeric variables. Proportions were compared with the Pearson chi-square test or the Fisher test, as appropriate. The level of statistical significance was set at  $P < 0.05$ .  $P$  values between 0.05 and 0.10 were considered borderline significant.

## 3. Results

### 3.1. Demographics

The average age of women at enrolment was  $31 \pm 1.4$  years (range 18–43). Based on occupation, 39.6% of the women were housewives or unemployed and 60.4% were employed. Regarding the obstetric history, 65/114 women (57%) were nulliparous, 44 (38.6%) were pregnant for the second time and 5 (4.4%) were multiparous.

### 3.2. Fish consumption and multivitamin supplementation

One hundred and four women (91.2%) consumed fish with an average frequency of 4.7 times per month. Each fish meal consumed averaged 150 g.

Nineteen women (16.7%) consumed fish 0–1 time per month, 61 (53.5%) women 2–4 times per month, 26 (22.8%) women 5–8 times per month, 8 (7%) women more than 9 times per month (Fig. 1, left panel). Distribution of women based on type of fish consumed is shown in Fig. 1, right panel.

Regarding multivitamin supplementation (data not shown), 59 women (51.8%) were taking supplements containing DHA (200 mg/day), and 55 of them (93.2%) were fish eaters. In addition, 101 (88.6%) reported folic acid supplementation, 91 (79.8%) iron

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